Volume 33 Spring 2017

MURJ

Massachusetts Institute of Technology
Undergraduate Research Journal

Feature p. 14

Interview: Nobel Prize Winner Bengt Holmstrom

Feature p. 22 *(on cover)*

7 New Exoplanets: Searching, and Spurring Innovation

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MIT URJ

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solving the toughest problems in life science

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Massachusetts Institute of Technology

UNDERGRADUATE RESEARCH JOURNAL
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Dear MIT community,

We are delighted to present the 33rd issue of the MIT Undergraduate Research Journal, a biannual student-run publication that showcases the exciting and diverse undergraduate research happening on campus. Since publishing its first issue 16 years ago, MURJ has represented the intellectual curiosity and passion of MIT undergraduates. In this semester's issue, you will read research articles covering a wide range of topics. This includes a study on the distribution of neurons in an area of the brain that is thought to play a role in aversive motivation, another report on GAMA, a model created to help designers plan more prosperous cities, and a third report investigating the criticality and supply risk of germanium, a common byproduct of zinc and coal.

In addition to our research articles, we also present insightful features articles that explore exciting scientific topics and happenings around the Institute. In this issue, we present an interview with Professor Bengt Holmstrom, winner of the 2016 Nobel Prize in Economics. We also discuss the growth of online learning platforms at MIT, such as edX, among many others. Lastly, we take a look at a team of MIT scientists trying to identify Earth-like exoplanets, and sit down with one of the team's members, Postdoctoral Associate Julien de Wit.

Biannual publication of this journal is a collaborative undertaking by an extraordinary team of dedicated students. We would like to thank our editorial board and contributors for their time and hard work this semester. In addition, we would like to thank all the undergraduates who shared their research with us and the greater MIT community.

Massachusetts Institute of Technology

MURJ Staff
MIT Undergraduate Research Journal

For previous issues of the MIT Undergraduate Research Journal, please visit our website at murj.mit.edu. If you are interested in contributing to future issues of the MIT Undergraduate Research Journal, we invite you to join our team of authors and editors or submit your research for our Fall 2017 issue. Please contact murj-officers@mit.edu if you have any questions or comments.

Best,

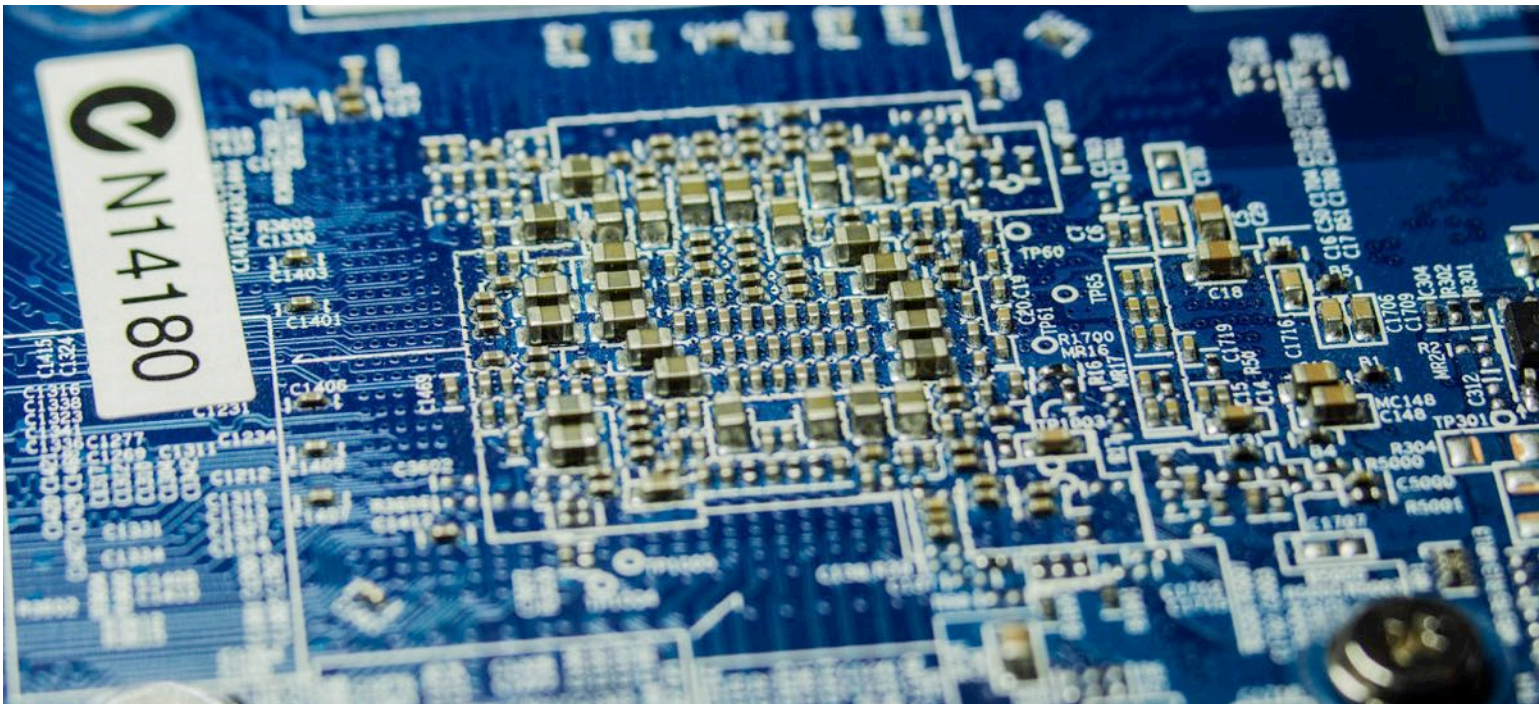
Elena Polozova
(Co-Editor-in-Chief)

Daphne Superville
(Co-Editor-in-Chief)

Massachusetts Institute of Technology

UNDERGRADUATE RESEARCH JOURNAL
Volume 33, Spring 2017

TECHNOLOGY



Manipulating Electronic Valleys for Novel Computing Technologies

Current computer hardware is based on the charge of an electron, and spin, another property of electrons, has also been a research focus for developing more powerful computing technology. The valley index is yet another property of electrons that has caught researchers' eyes as a possibility for creating more powerful computing technology.

The valley index is determined by the relation between the energy of an electron and its momentum. Materials such as tungsten disulfide have two electronic "valleys," distinct energy states in which electrons gather as they travel through the material. Little is known, however, on how to manipulate these electron valleys, which is important for the data manipulation required in computers. A recent study in the Gedik Lab of the Department of Physics demonstrates the use of light to tune the electron valleys.

Interactions with off-resonance light can lead to shifts in atomic energy levels due to two effects: the Stark shift and the Bloch-Siegert shift. While the Stark shift has a large, easily observable effect, the Bloch-Siegert shift is typically less than 1 μeV, so it is rarely observed. Usually, these effects occur together, adding to the difficulty of disentangling the two shifts. In a recent paper in *Science*, researchers led by Nuh Gedik observed a notably large Bloch-Siegert shift in tungsten disulfide (WS2), the first observation of the effect in a solid.

In WS2 the two electronic valleys lack inversion symmetry, which leads to different optical selection rules for the valleys. Since the Stark shift and Bloch-Siegert shift are time-reversed partners, tungsten disulfide allows the two effects to be separated, because they occur in different valleys rather than occurring in the same place. Indeed, an earlier study found that shining left-polarized visible light on WS2 changed the energy levels of electrons in one valley but not the other. This time, the researchers used infrared light.

Gedik and his colleagues used femtosecond pump-probe absorption spectroscopy to pump an atom-thick layer of tungsten with infrared light rays and measure the shift of energy in each valley. They varied the pumping photon energy and saw that at higher energies, there was a signal corresponding to the Stark shift at one valley and a weak signal at the other valley. At lower energies, however, the signal became comparable in strength, and the Bloch-Siegert shift they observed was 1,000 times stronger than what had been observed previously.

The separation of the Stark shift and Bloch-Siegert shift in the two electronic valleys allows for the manipulation of the energy levels of the two electronic valleys independently. Such a manipulation enables researchers to move electrons from one valley to another, which could facilitate the manipulation of valley index required for valley-based computing devices faster and more powerful than modern computers.

—Jordan Hines

BIOLOGY

Quantifying a Critical Molecule in Malaria-Causing Parasites

In the 2015 World Malaria Report, the World Health Organization estimated 214 million cases of malaria, resulting in 438,000 deaths, many of which were caused by the human malarial parasite Plasmodium falciparum. Some of the most successful treatments for malaria, including chloroquine, belong to a class of drugs that interact with the heme molecule, a cofactor that is important to cellular processes including energy production and oxygen transport, but that can be toxic to the parasite at high levels.

MIT researchers from the Department of Biological Engineering have developed a genetically encoded fluorescent protein heme sensor, allowing them to quantify the level of heme normally maintained in live P. falciparum parasites and demonstrate the effect of parasite exposure to chloroquine on heme concentration. The study was published in the Proceedings of the National Academy of Science and authored by James Abshire, Christopher Rowlands, Suresh Ganesan, Peter So, and Jacquin Niles.

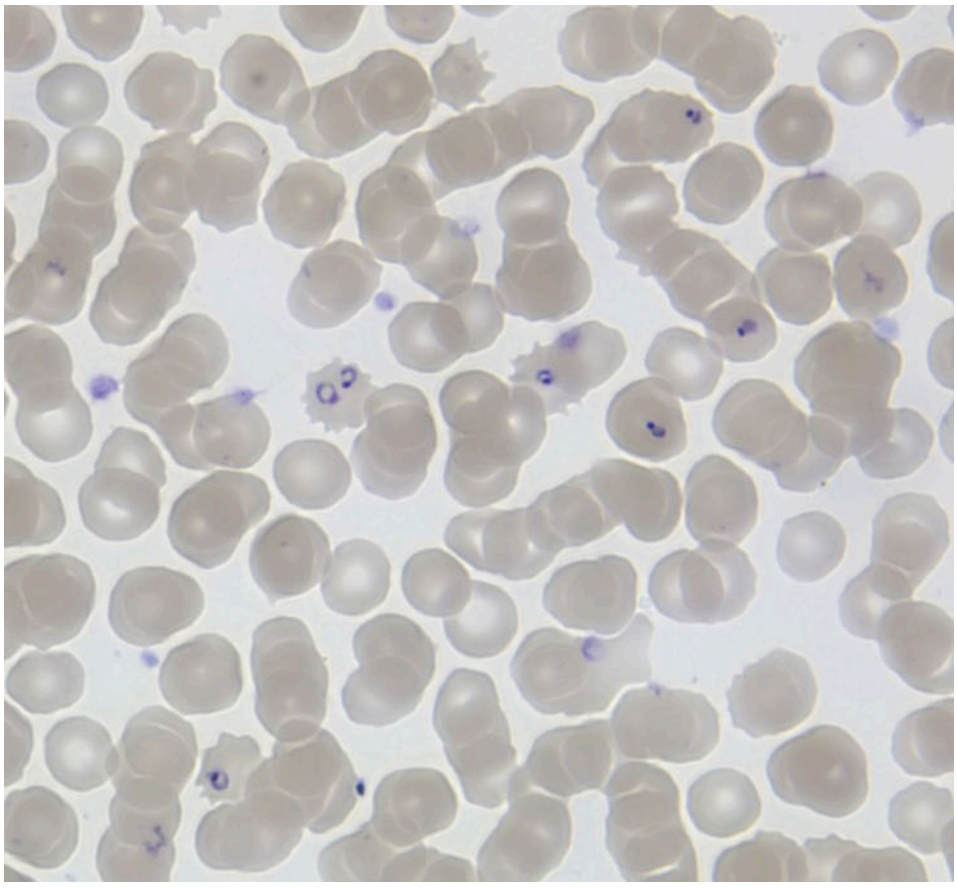
Previous methods for sensing heme levels required lysing the cells of the parasite, which makes it difficult to determine the subcellular location of heme, or measuring enzyme activity dependent on heme rather than heme itself. However, the genetically encoded heme sensors developed for the MIT study facilitate the direct quantification of heme levels and determination of heme distribution in an intact parasite.

When P. falciparum infects human red blood cells, it takes up and digests 30-70% of the cell's hemoglobin, releasing peptides and heme. Most of the heme is converted into a relatively inert crystalline form called hemozoin to protect the parasite from heme's damaging reactivity, while some is maintained in a labile pool at a concentration of 1.6 μM. The study found that even as P. falciparum parasites degrade more hemoglobin as they progress through their development cycle, the labile heme level remains relatively stable.

Antimalarial drugs like chloroquine are proposed to function by inhibiting the crystallization of heme into hemozoin when the parasite digests hemoglobin, increasing the concentration of heme in the cell to toxic levels. This study lends support to this proposed mechanism of action, demonstrating that labile heme concentration in malaria parasites increases significantly after exposure to chloroquine by quantifying heme levels using genetically encoded biosensors.

These heme biosensors allow researchers to better quantify levels of labile heme in P. falciparum and better understand the mechanism of action for antimalarial drugs like chloroquine. Chloroquine resistance in P. falciparum is widespread, but according to the authors of the study, better understanding how drugs like chloroquine kill parasites "could potentially be exploited for developing the next generation of antimalarial drugs that are not immediately compromised due to cross-resistance."

—Allison Huske



Plasmodium falciparum inside red blood cells
(Source: Wikimedia Commons, Photo credit: Michael Zahniser)

OPINION

Treating Endometriosis

An agonizing disease that affects millions of women worldwide

"I am a mom, a warrior," a term Nicole Pearlstein uses to describe anyone who has had endometriosis, "and I am the mom of a fourteen year old warrior... She is what drives me to continue this advocacy everyday." Later when Nicole asks for all of her sisters to stand, her daughter is among the majority of women present who rise in a yellow flourish—like pink represents breast cancer, yellow is the rallying color for endometriosis. "These... are the most resilient, strongest, bravest women you will probably ever meet in your lifetime."

Across from the Boston Commons at the Hampshire House, an endometriosis panel was held the morning of March 25th, followed by a march on the Boston Commons. The panel included Julia Sales, a mental health specialist, Casey Berna, a social worker and endometriosis advocate, and the only known endometriosis excision specialists in New England, Dr. Malcolm W. "Kip" Mackenzie and Dr. Martin Robbins. Dr. Mackenzie is stationed at Mount Auburn Hospital, while Dr. Robbins is from Maine at Advanced Women's Health Care & The New England Center for Endometriosis. The main goal of the panel was to provide an interactive discussion with the audience about endometriosis, a disease that affects one in ten women and can cause severe, debilitating pain to the abdomen.

According to Nicole, one of the coordinators of the panel, endometriosis is "the most common disease no one has ever heard of," even though it affects 176 million women worldwide and accumulates 119 billion dollars nationwide in healthcare costs every year. More technically, endometriosis is when endometrial tissue—tissue that lines the uterus—localizes outside of the uterus. It can develop on the colon, intestines, stomach, appendix, etc., and thus can cause pelvic inflammatory disease, digestive problems, and other issues, including excruciating pain. Endometriosis causes fatigue, increases anxiety and depression, and has also been associated with infertility. It affects people's relationships and as such is a bane on the patient's social life. Treatments for endometriosis were discussed at the panel. Excision specialists talked about what is considered the definitive method for treating endometriosis. Some say hysterectomy and bilateral salpingectomy, removal of the female reproductive organs. Others say there is no cure for endometriosis but ablation, where the doctor either laser beams, electrocutes, freezes, or heats the endometriosis, is a patient's best option. When the patient comes back two years later because the endometriosis has come back even worse, they are not surprised since "there is no cure for endometriosis." Even the drug Lupron, which removes estrogen from the body, was described as "borderline abusive" by a warrior at the panel who had hot flashes, night sweats, and forgot details while on Lupron.

Removing the female reproductive organs, according to Dr. Robbins and Dr. Mackenzie, does nothing

Endometriosis March on the Boston Commons after the Endometriosis Panel on March 25th. (Source: Nicole Pearlstein)

Endometriosis March on the Boston Commons.
(Source: Nicole Pearlstein)

if the endometriosis is left behind. Since endometriosis can produce its own estrogen, it just keeps on building and shedding, regardless of if the reproductive organs are present or not. It is for this same reason that Lupron is ineffective. In 61% of cases, endometriosis is more than two millimeters deep into the tissue. Ablation only removes endometriosis up to two millimeters deep, so endometriosis roots are left behind in the vast majority of cases. For this reason, patients undergo repeated ablation surgeries, a process that often causes recurring pain and inflammation.

The method that Dr. Robbins and Dr. Mackenzie find most effective is excision surgery, where a surgeon laparoscopically cuts out the endometriosis from the body. The procedure generally takes at least four hours and if every bit of endometriosis is excised, the endometriosis does not come back.

Later, Casey asked the audience, "How many of you have had ablation?" Several hands went up. "Out of you who had ablation as first treatment, keep your hand up if that healed you and made you better?" Everyone's hands went down. Then Casey asked, "How many of you have had excision?" The majority of hands in the room went up. "How many of you had gotten some relief from excision?" There were smiles on the women's faces all across the room, as they kept their hands in the air.

There are only 100 excision specialists worldwide for a disease that affects 179 million women. According to excision specialists, it does not help that future doctors are being taught the wrong methods for treatment of endometriosis. It does not help that the average diagnosis time from the onset of symptoms is seven to ten years. What we need is more research to prove that the methods these 100 doctors use is the best method we have thus far. What we need is a substantial increase in funding for endometriosis research that could benefit labs like Dr. Linda Griffith's MIT Center for Gynepathology Research. Funding would also be beneficial for methods like the endometriosis diagnostic tool, manufactured by the MIT iGEM team, that was discussed in our previous issue.

At the end of the panel, the attendees went out to march on the Boston Commons. I can still see the yellow hope that their tears, their cries, their pain would be heard and answered for. Because most of all what we need is greater awareness of this disease so that women, teenagers, and young girls do not have to suffer through the "evil," as Nicole would say, that is endometriosis.

— Ayse Guvenilir

MEDICAL TECHNOLOGY

Hacking Healthcare & Demystifying Diagnostics

As medical technologies centered around patient care and use started to explode, more and more medical devices have essentially become expensive "blackboxes" that cannot be modified or recreated by the user. The focus of the Little Devices Lab at MIT is to create community based projects and devices that allow the user to solve their own problems by hacking with the materials around them. Currently, the lab is approaching this goal with two distinct yet interconnected projects: Asynchronous Modular Paperfluidic Linear Instrument-free block (AMPLI) and MakerHealth.

AMPLI is a modular diagnostic system that allows people to assemble their own diagnostic tests by connecting Lego-like building blocks on a board. Unlike standard diagnostics, AMPLI allows the user to customize a variety of diagnostic tests that would traditionally be performed with pipettes or tubes. In fact, the lab is in the process of publishing a paper regarding AMPLI's low cost modular diagnostics system. Jose Gomez-Marquez, one of the co-directors of the lab, explained the concept of this technology in analogy to the development of the breadboard. A big jump from the complicated electrical circuits in the 1920s, electrical engineers invented the breadboard in an effort to allow anyone to intuitively modify and assemble their own circuits. Similarly, Jose believes that AMPLI is a biological "breadboard" that "demystifies how many of today's diagnostic tests are built and performed."

Not only does the lab build tools for others to hack diagnostics, they also build spaces around the country to cultivate a hacking environment in hospitals. Unknown to many, medical innovations are constantly developing around us, not just by researchers and companies, but by nurses and technicians who work closely with the users – patients. MakerHealth is a spin-off company of MakerNurse, a research project in the lab that focuses on the "prototyping genome" of inventive nurses in the United States who are hacking away in the hospital supplies closets to improve patient care. According to Anna Young, the co-director of the lab, MakerNurse drew its inspiration from MIT Sloan Professor Eric

The MakerHealth Space is a place for the UTMB community to design, build, and prototype.
(Source: UTMB)

Zika Virus Vaccine

As of February 2016, the World Health Organization has declared the recent Zika virus (ZIKV) outbreak a Public Health Emergency of International Concern. Zika virus is a mosquito-borne flavivirus that has been associated with birth defects such as microcephaly and Guillain-Barre syndrome, among other neurological complications. Since the beginning of the most recent outbreak in Brazil in 2015, the incidence of cases has only continued to increase throughout the globe.

In response, researchers at the Koch Institute for Integrated Cancer Research and the Whitehead Institute for Biomedical Research have developed an RNA-based vaccine candidate. In a paper published in Scientific Reports, first and second authors Jasdave Chaval and Tao Fang, along with senior author Hidde Ploegh, describe their RNA-based vaccine candidate.

The vaccine candidate builds upon previous research done by the same group that resulted in RNA nanoparticle vaccines against lethal influenza, Ebola, and Toxoplasma gondii in mouse models. It consists of a nanoparticle containing messenger RNA, or mRNA. When the mRNA is inserted into the body, it is translated into viral proteins that provoke an immune response. In the case of this ZIKV vaccine, the proteins the mRNA encodes are those from the virus' premembrane and envelope, proteins that would not cause harm to the animal, but are an indication of ZIKV's presence to the immune system because they form the membrane that surrounds the harmful genetic material ZIKV carries.

Mice were injected with the RNA nanoparticle vaccine, and then their CD8+ T cells, or killer T cells, were extracted. These T cells, which mediate the immune system's adaptive response to pathogens, were exposed to a library of ZIKV viral proteins in order to gauge the effectiveness of the vaccine. The T cells of immunized mice responded to an amino acid sequence that codes for a ZIKV envelope protein. This finding was surprising, given the sheer size of the ZIKV genome and the myriad proteins it encodes. According to the researchers, the amino acid sequence isolated in this study is conserved across all known genetic variants of ZIKV, making it a viable standard of measure for the efficacy of future vaccines. They also note that the development of their vaccine only required access to ZIKV's coding sequence, not to the virus itself, unlike other ZIKV vaccines.

A DNA-based ZIKV vaccine is currently in clinical trials, but according to Chaval and colleagues, the "self-limiting nature of an RNA-based vaccine possesses obvious safety advantages over DNA-based approaches," mainly because the RNA-based vaccine cannot integrate into a patient's genome.

— Nafisa Syed

Von Hippel's research on lead user innovators. Lead user innovators are people who modify different devices to fill a need, and end up being ahead of the product development curve.

From a nurse who 3D printed a clip to hold more IV tubes to the neurosurgeon who 3D printed a stabilizing head gear, MakerHealth is fostering a hacking community of user innovators composed of nurses, clinicians, physicians, and staff by installing makerspaces in hospitals. Like makerspaces for students on MIT's campus, these makerspaces allow thousands of hospital staff members to hack and produce prototypes to suit their needs. By installing a makerspace directly inside the hospital, MakerHealth changes the environment of these hackers to quickly prototype any idea that comes to mind and share it with the world. The vision of MakerHealth is to ensure every hospital in the U.S. has a makerspace that can allow innovators to make immediate impact on the lives of their patients.

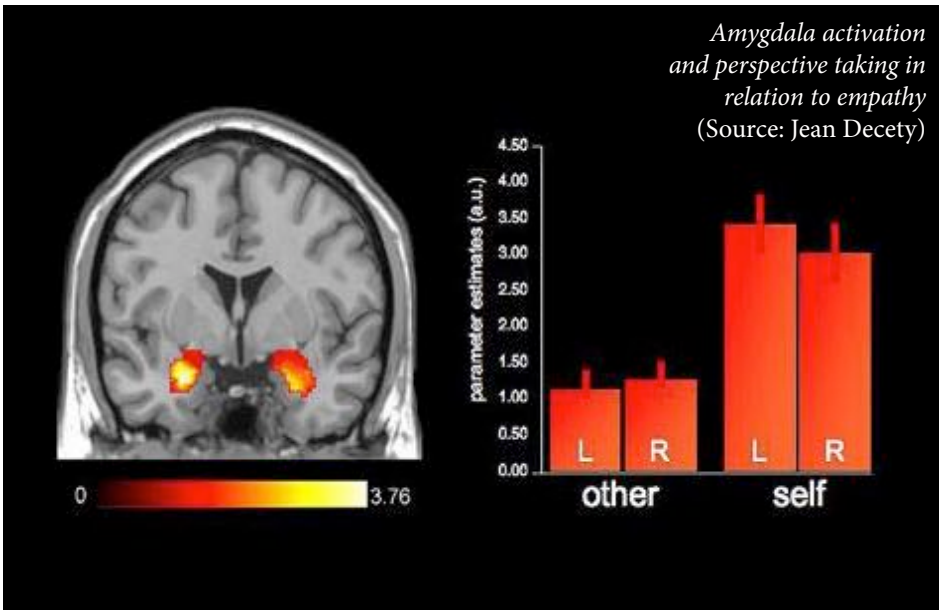
The Little Devices Lab is an embodiment of MIT's motto, "Mens et Manus"—"mind and hand." The lab not only produces technologies, it produces the tools enabling users to make technologies as well. As our environment becomes increasingly filled with "user friendly blackboxes," the Little Devices Lab provides us with insight into how these technologies function and how we can modify them to suit our health needs.

—Zulkayda Mamat

NEUROLOGY

More Than Fear

Researchers reveal the amygdala contains reward circuitry



Amygdala activation and perspective taking in relation to empathy (Source: Jean Decety)

The amygdala, a brain structure that has long been associated with anxiety and fear, may in fact be involved in reward-seeking behaviors. Researchers in Susumu Tonegawa's lab at the RIKEN-MIT Center for Neural Circuit Genetics at The Picower Institute for Learning and Memory in collaboration with the Department of Biology and the Department of Brain and Cognitive Sciences discovered five populations of neurons within the central amygdala that mediate positive behaviors. Joshua Kim and Xiangyu Zhang are the lead authors of the resulting study, which was published in *Neuron*.

This study builds upon a previous study from Tonegawa Lab that examines the basolateral amygdala (BLA) and its role in negative and positive emotions. The BLA connects directly to the central amygdala, so researchers decided to examine seven genetically distinct neuron populations in the central amygdala in an effort to better understand these connections.

In order to determine the function of each neuron population in mice, the researchers used optogenetics, a procedure in which neurons are stimulated via exposure to light. Each neuron population was initially activated in a controlled environment to determine the mouse's baseline response, and then each mouse underwent a self-stimulation task, where it was allowed to freely choose between two ports. One would activate a neuron population by shining light, while the other had no light, and so would not activate any neurons. Mice chose to activate five of the seven neuron populations, indicating that these five populations are involved in positive motivation.

The mice were also exposed to water and food deprivation, as well as footshock conditions, and the subsequent activity of the seven neuron populations was monitored by examining gene expression. In particular, researchers measured the activity of the Fos gene, whose expression correlates with neuronal activity. They found that the five neuron populations associated with positive motivation isolated earlier were also active in the mice with enough food and water, confirming these neurons' involvement in a reward circuit.

The neuron populations that the mice chose to activate, incidentally, all connect to the cells mediating positive emotion in the BLA. Of the remaining two neuron populations examined, one appears to mediate negative or fear-related behaviors, in line with the traditional view of the amygdala. The other, however, seems to have no role in either fear-averse or reward-seeking behaviors.

Even the researchers' discovery of neurons involved in a fear circuit challenges previous conceptions of the amygdala: these fear-related neurons do not connect to the periaqueductal gray (PAG), a brainstem structure responsible for stress response. The amygdala was thought to project connections directly to the PAG in order to drive this response to aversive stimuli, but this does not seem to be the case. Tonegawa's lab plans to further investigate these connections, along with the connections of the reward-mediating central amygdala neurons. As they gain an understanding of the various circuits of the amygdala, Tonegawa and his colleagues may shed light on conditions associated with fear and lack of motivation, such as depression, anxiety and post traumatic stress disorder.

—Nafisa Syed

MURJ Features

MIT Department of Economics

MURJ Spotlight: Bengt Holmstrom

This issue's spotlight features Professor Bengt Holmstrom, a professor in the Department of Economics and a 2016 Nobel Prize Winner.

By AMAN PATEL

MIT Professor Bengt Holmstrom inspired the MIT community by winning the 2016 Nobel Prize in Economics along with Harvard Professor Oliver Hart. The prize represents the culmination of decades of work related to contract theory – the interplay between the content of contracts and the resulting influence on people's incentives to complete their work. The key to contract theory is incentive, and Holmstrom's contributions focus on the needs to balance incentive with risk. His work allows us to better understand and design better contracts.

Professor Bengt Holmstrom has been at MIT for nearly 23 years studying and teaching economics.

(Photo credit: Bryce Vickmark)

OVERVIEW

When he graduated from college, Dr. Bengt Holmstrom said he never envisioned becoming an economist at a university. In fact, he initially worked as an operations researcher for a large Finnish corporation, tasked with implementing a model to optimize output. He soon realized the exercise was fairly pointless as the data he was using lacked critical information, especially relating to employee incentives. Dr. Holmstrom said that this was the first time he really started to think deeply about the problem of incentives. It remained in the back of his mind, however, until he received a Fulbright Grant to complete his Masters in Operations Research at Stanford. While completing this degree, he said he found that incentives were becoming a "hot topic" in economics. In his words, he saw lots of "low-hanging fruit" to study. He eventually received calls from several notable schools, including Harvard, Yale, Northwestern, and Carnegie Mellon, and chose to take a teaching post in economics at Northwestern. While there, he started studying incentives and contract theory in earnest. He later moved to Yale, and in 1994, he accepted a position at MIT, where he has worked ever since.

The Nobel Prize is awarded for in physics, chemistry, Medicine, Literature, Peace, and Economic Sciences.

(Photo Credit: nobelprize.org)

Dr. Holmstrom cited a variety of reasons that drew him to MIT, including MIT's high rank in economics, personal connections, and the intellectual environment created by the several top schools in the area. A school's students make a significant contribution to this intellectual environment, a fact that is not forgotten by Dr. Holmstrom. He especially holds

Professor Holstrom spoke about his work at an on-campus press conference on October 10th.

(Photo Credit: Bryce Vickmark)

a passion for his role as an undergraduate advisor and makes it a point to accept as many advising assignments as possible. Dr. Holmstrom stressed that students shouldn't cling to preconceived notions about their future paths. He said, "You (students) are here, in my view, to find out what you are excited about." He further believes that students should "explore" instead of "assuming whatever you were conditioned to do." "College is a journey of who you are and what you might like," he said. This journey continues through any future career, as "the world today is open; it almost forces you to explore." In a time where students struggle to find their true passion, this advice is certainly refreshing.

Even with a Nobel Prize, Dr. Holmstrom certainly isn't done. He acknowledges the platform this prize has given him, but he has no interest in using it to "pontificate about the world." Instead, he said he hopes to use it to benefit the MIT community and the world. He plans to focus more on advising students, and he is also considering continuing his Nobel-winning research on contract theory and incentives as he has mainly focused on other areas in recent years. He also would like to branch out into other academic interests, including executive compensation or the behavioral aspects of economics.

Despite his groundbreaking work, Dr. Holmstrom said he certainly wasn't expecting to win a Nobel Prize this year. He knew he was a strong candidate if the Nobel committee decided to give the prize for contributions to contract theory, but there was a myriad of economic fields in which the prize could have been awarded. He compares it to "putting money on one number on the roulette table." No matter how accomplished one is, there are "many more names than prizes." He received the call at 4 AM while on antibiotics for oral surgery, and his initial thought was that his alarm to take the next dose had been left on by accident. Instead it was phone call letting him know that he won the Nobel Prize. Dr. Holmstrom describes the Nobel ceremony – complete with his friends, relatives, and the Swedish royal family – as "unforgettable." He cheerfully notes that he's "going to live off that for a very long time."

Through his research and advising, Dr. Holmstrom has made an indelible mark on MIT. His passion for his students and work certainly stands out, and his unconventional story is one everyone can learn from. His Nobel Prize is truly a mark of pride for the entire MIT community.

INTERVIEW

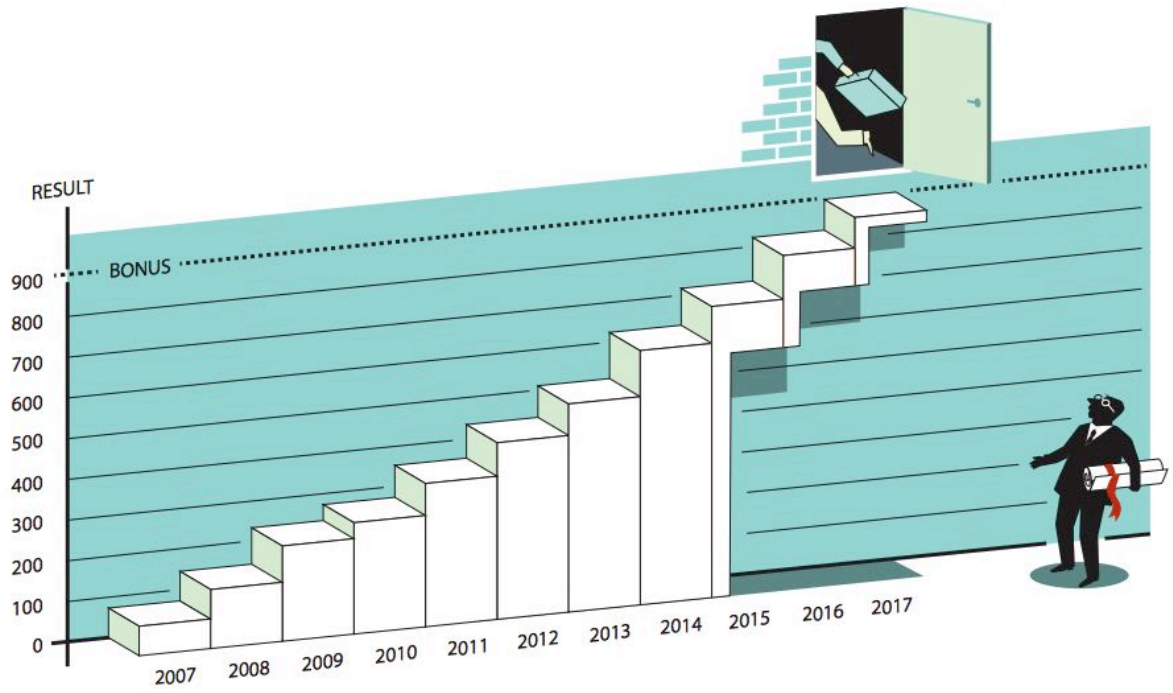
What is your story about getting the news that you had won a Nobel Prize, and what was your reaction?

I think they call around 4:15 or 4:30 in the morning. I had an infected tooth at the time, and I had just taken my antibiotics. I thought somehow the alarm had been left on for that, so I was completely confused when I answered. It was definitely a big surprise – you don't really expect it; it's like having your money on one number on the roulette table. I would say that if the prize came in this field, then I knew that I was an important contributor, but I was not at all sure they would give it in the field. Certainly, the timing of Nobel Prizes is very unpredictable. You look at who could get it within the next ten years, and there are certainly more names than prizes. Frankly, there are people who are just as deserving or even more deserving. But yes, it was very surreal in a sense. You sort of feel a little dazed. Also, Stockholm (capital of Sweden where Nobel Prizes are awarded) was wonderful. That week (of the Nobel Prize Award ceremony)– it's a whole week of celebrations – it's a fantastic week. You have your relatives and friends around, and the royal family's there. I've participated before, but when it happens to you, it's a whole different experience. I'm going to live off that for a very long time.

What first drove you to become interested in contract theory and economics in general?

I had an unusual route in the sense that I worked for two years. I was an operations researcher and was assigned to implement a huge linear programming model for a large company. We're talking thousands of variables and hundreds of equations, which is very complex. At the time, computers had just become more widely used, and there was the hope that these programs would become instrumental in their strategic plans. I realized the information for these programs was very obviously biased, and I felt this whole exercise was practically meaningless. I started to work with incentives, payment schemes, and pay for performance (in attempts to rectify this).

You initially worked at a company, so what brought



Holmstrom's multi-tasking model shows that if a manager's performance pay emphasizes short-term cash flow, his actions may neglect the company's long-term health.

(Photo Credit: nobelprize.org)

MIT President Reif congratulated Professor Holmstrom at the press conference following the announcement of his win.

(Photo Credit: Bryce Vickmark)

you to a university and eventually to MIT?

I went on a sabbatical from my firm – I got a fellowship to come to the US to study operations research. I planned that I would maybe become a better operations researcher, but I always had incentives in the back of my mind. I did get my masters in operations research, but then I hooked up with Stanford business school and realized that incentives were becoming a hot topic in economics. So I shifted into thinking about economics. Initially, from an operations research perspective, these models seemed very naïve, and I had a hard time seeing how they could be significant. But it takes time to understand that economic modeling is about what you can leave out and still have something interesting, not what you can fit in and be able to solve the problem, which is the mindset of an operations researcher. I then went back to Europe, which was a condition of my Fulbright grant. I soon got job offers from Carnegie Mellon, Yale and Northwestern, and I chose Northwestern because that's where many of the people I knew from Stanford were situated. Then I got an offer from Yale and went there, and 22 years ago, in 1994, I came here.

How would you describe the intellectual environment here, and what drew you to MIT in the first place?

Well, first of all, it has been consistently the highest ranked department. I also knew several people here, and there's also Harvard and BU nearby, so this is an important area for economics. My son had also gone to college. I had gotten offers from Harvard and MIT before, but I had not been inclined to go while my son was still home. Yale itself is a great place for economics, but when Paul Milgrom left, it wasn't so good for me anymore. Paul Milgrom is a very critical collaborator – if you take away the work I did with him from my CV, I'm sure there would be no Nobel Prize.

At MIT, students here are just starting out their careers. What advice do you have for them, and are there any lessons you have learned that may be useful?

Every student is different. I like to be an undergraduate advisor, and I like to hear who you are and what you are interested in. Generic advice, I think, has its dangers. You are here, in my view, to find out what you are really excited about. That's one of the great things about the US system – students come here and they can change fields within the four years. I would say take advantage of that. My first order of business would be to explore, and MIT forces you to do so. It's a journey of discovery of who you are and what you might like. One doesn't have to be stressed out for not knowing. One should be curious and do things they find interesting. Students should be less concerned about the grade point average and things like that. When I read transcripts from a student who just has A's everywhere – from history to mathematics – that student is not necessarily as interesting to me as one who has all A+'s and maybe a C in something. That shows a strong interest to me. There's always something that makes a student special, and I would look for that. It's about taking risks, not seeing where you can get the most money. The world is so open that it almost forces you to explore.

What's next for you?

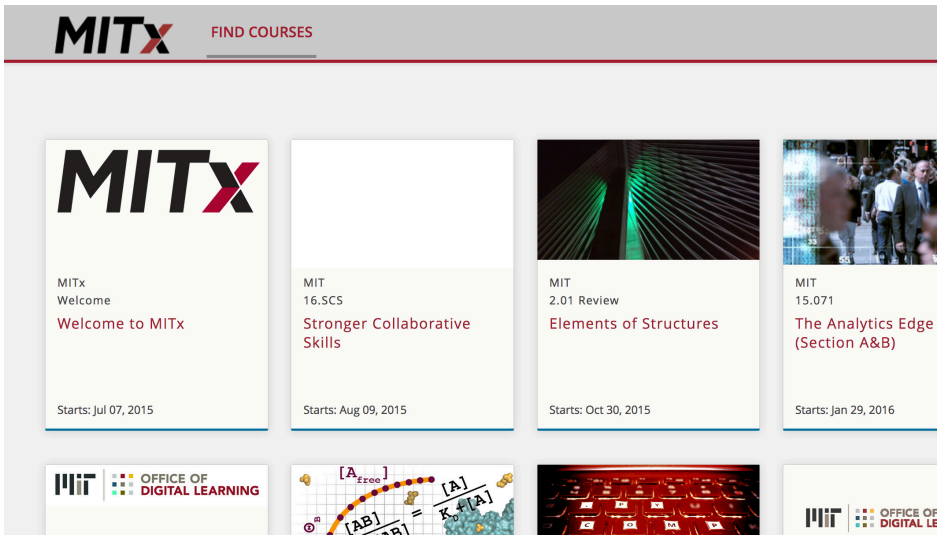
I haven't really thought about it very much. Some people take (the Nobel Prize) as a very big platform. I guess I want to utilize my platform in some manner – I don't have interest in pontificating about the world. I'm very interested in young people, so I take almost all the undergraduate advising assignments that I am asked for. Then I'll study. I'll continue to stay abreast with understanding the financial system. I actually stopped working actively on incentives around 20 years ago, so I may get back into it after all these years, maybe studying executive compensation or the behavioral aspects of economics. ▪

The MIT Sloan School of Management, where Professor Holmstrom holds a joint appointment.

(Photo Credit: Moore Ruble Yudell Architects & Planners)

Behind the Screens of Online Education

BY THERESA MACHEMER

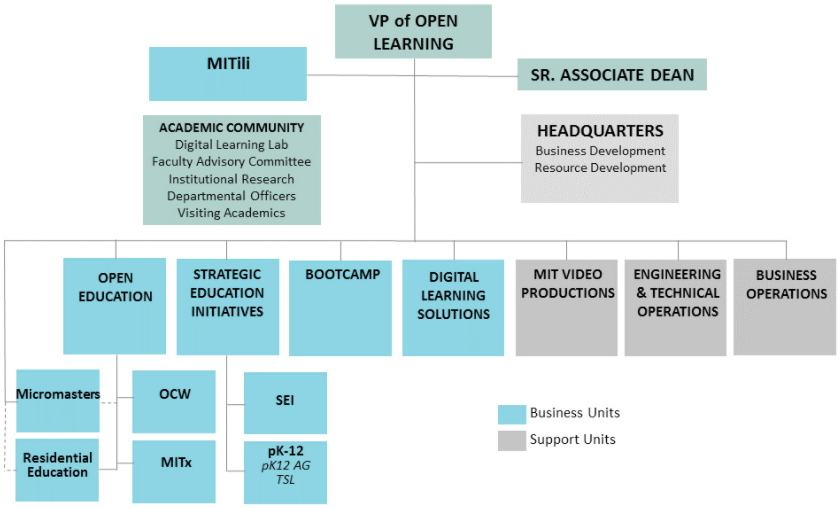


MITx is a platform where online content for many MIT classes is integrated with what is taught in the classroom.

(Photo Credit: lms.mitx.mit.edu)

MOOCs, or Massive Open Online Courses, have been around for nearly ten years and have in that time become almost ubiquitous in higher education. The first MOOC, "Connectivism and Connective Knowledge/2008" was launched in 2008 by the University of Manitoba, Canada, leading the way before MIT and Harvard affiliates launched a nonprofit, open source MOOC platform, edX, in 2012. Nearly every MIT undergraduate has experienced MOOC content, whether they realized it or not, because the general institute requirements Classical Mechanics (8.01), Electricity and Magnetism (8.02), and some versions of Introduction to Biology (7.01x) have an online module through MITx that integrates MOOC content with their MIT-specific components. And we can't forget the number of classes that MIT has available through OpenCourseWare, most complete with lecture videos, problem sets, and exams, good for reviewing class material or learning something new. When material is available online, it can be easy to ignore how it came to be there. Maybe we assume that it's re-used year to year, or that it's managed by a few teaching assistants, or we don't think about it at all, but in fact MIT has an entire department committed to creating, maintaining, and researching effective educational materials online. It's called the Office of Digital Learning, or ODL.

The Office of Digital Learning was established in 2013 with a mission "to support and empower MIT faculty as they reimagine and reinvent education in the digital age," according to the ODL website. The educational content in an edX or MITx course, for example, is now often created by MIT faculty

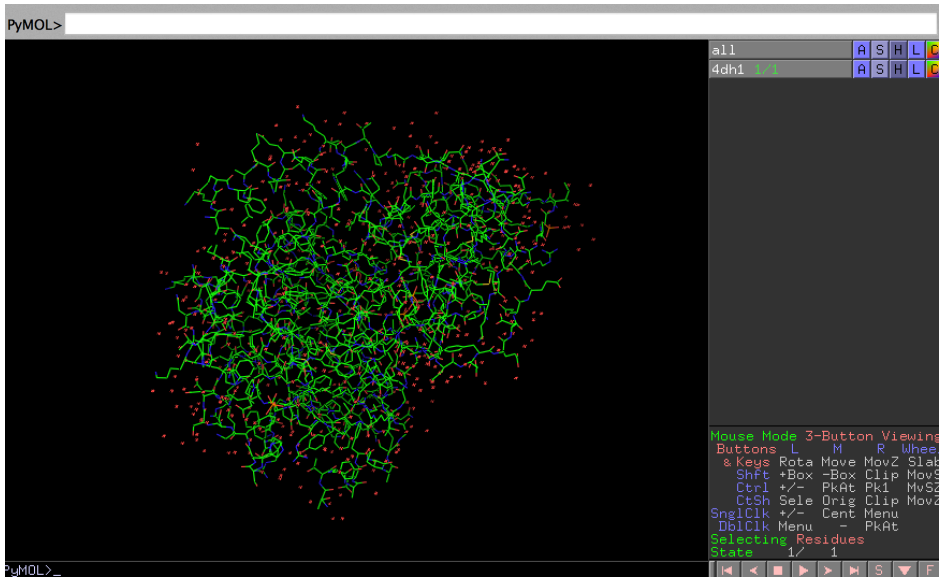


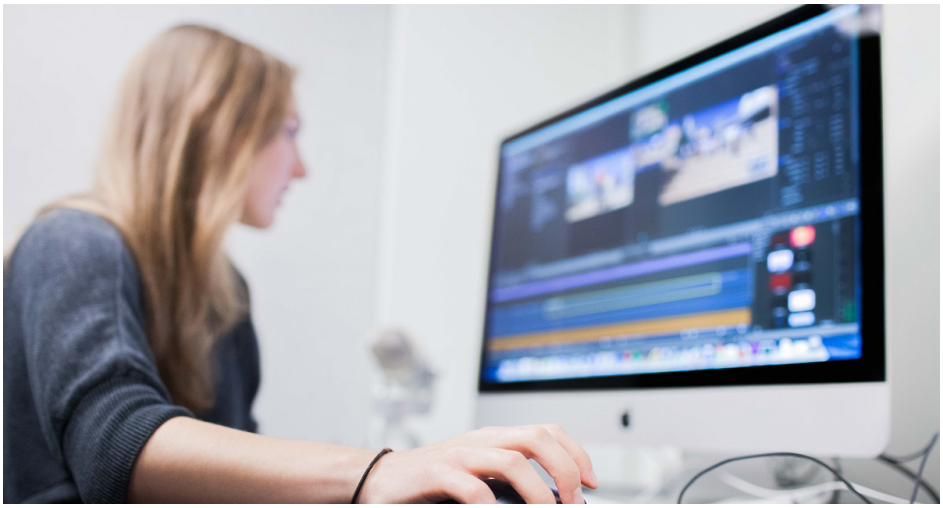
The organizational structure of the Office of Digital Learning (ODL).

(Photo Credit: odl.mit.edu)

working closely with the scientists and fellows of the Digital Learning Lab (DLL), officially established in 2015. DLL members are experts in the discipline of the course as well as in teaching, research in education, and project management. Right now, only 8 departments—Mechanical Engineering, Materials Science and Engineering, Electrical Engineering and Computer Science, Biology, Physics, Urban Studies and Planning, Math, and Supply Chain Management—have DLL scientists or fellows, but with time that number will likely increase.

The MIT Biology department has two DLL fellows, Swati Carr and Sera Thornton, and one DLL scientist, Mary Ellen Wiltrout, all biologists with Ph.D.'s. They work in the back of the Biology education office, 68-120, by the conference room table that's often filled with TA's grading exams. "[The Digital Learning Lab's] model is very different than what a lot of other schools are using," Wiltrout said. "We know the science and we work with the faculty members to create the content instead of it being somebody who doesn't know biology, which at other universities can lead to a 'telephone' effect where the faculty must first teach the online course creator, who then tries to teach the online students. MIT's system is "a much more efficient partnership because we know the science, as well as the teaching techniques," Thornton said. The success of the Biology department's online courses, which includes all of the MITx modules of on-campus courses as well as edX offerings like an introductory course and a 3-part molecular biology course, has been





Top: In 7.05, PyMol is used to accompany psets so students can visualize amino acids and proteins.

(Photo Credit: author)

Bottom: MOOCs have provided educational material to areas previously without access.

(Photo Credit: MITx)

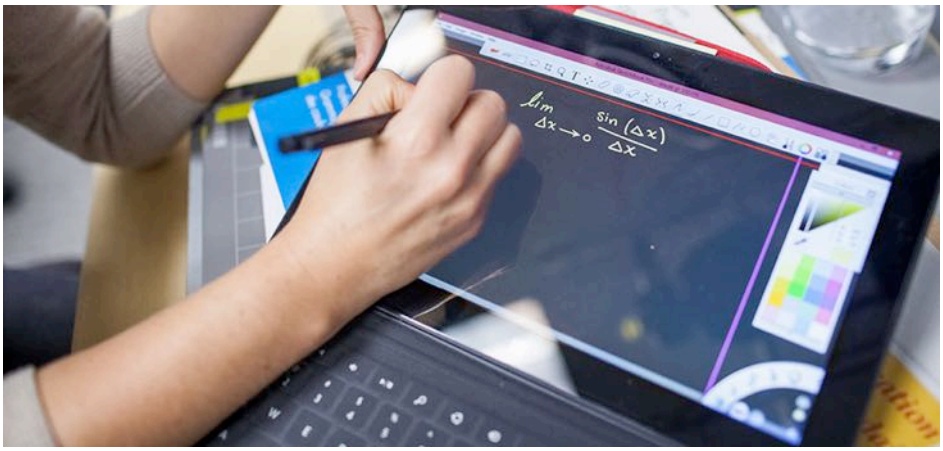
helped by the fact that two of the three Course 7 DLL members, Wiltrout and Thornton, are graduates of MIT themselves, having received their Ph.D.'s from MIT in 2009 and 2014 respectively, so they understand how the school and the students prefer to work. "That's important because—especially if we're creating things for MIT students to do—if we didn't understand how MIT students work, there could be major disasters." Wiltrout said.

Members of the Digital Learning Lab don't only make the content for online courses; they can do experiments in them too, by giving different versions of the content to different segments of the student population. They don't do this in the MITx courses—MIT students would certainly catch on—but in

an edX course of tens of thousands of people across the globe taking the course recreationally, there's a much lower chance of a student revolt. Testing parameters can include variations like the order in which material is presented, the kinds of exercises like multiple choice versus a drag-and-drop, or the style of informational video, like a video recording of a lecture versus a video specifically formatted to teach a concept, called a "deep dive." The Biology DLL group published a paper on the last topics, entitled "Criteria for Video Engagement in a Biology MOOC," authored by Thornton, Wiltrout, and an undergraduate researcher who joined the group through UROP, Ceri Riley. The edX platform records the clicks of students taking the course- a dataset called the clickstream- tracking characteristics like time spent watching a video so that educators at DLL can analyze huge volumes of data and track, for example, the success of "deep dive" videos versus lecture videos as reflected in engagement, measured by whether they completed the video having started watching it. Data can be further broken down by characteristics like video length, the amount of "face time" with the video host, and the perceived expertise of the host (in the case of a professor versus anonymous narrator). This and other MOOC research was presented at a conference called "Learning at Scale" at MIT. "We think it's really important not only to make these courses as good as we feel like we can make them, but also to look at the data and make sure that the courses are working the way we hope they are, and to share that knowledge that we've gained with the rest of the MOOC community and the MIT community," Thornton said.

When MOOCs first began to appear, headlines lauded them as the next revolution in higher education, claiming that they could make the traditional university system obsolete. MOOCs haven't fulfilled the promises of that early hype, and while some early supporters of MOOCs are now disappointed in the direction they've taken, Thornton is optimistic.

"What we're really learning is that, no, MOOCs aren't really going to replace the traditional, in-person college education. What they're able to do is provide learning experiences to people who want them who would not normally be able to access them," she said. The students in MIT's Biology MOOCs range from homeschooled middle school students, to students in rural India (usually 15-25% of learners identify themselves as being from India), to retirees who may be 40 years out from a formal biology education and want to see how the field has developed. "We're making a difference in the lives and educational opportunities of individual people in the world, and that's exciting." ▪



Digital tools allow students to interact directly with class material.

(Photo Credit: odl.mit.edu)

Worlds Apart, Worlds Within:

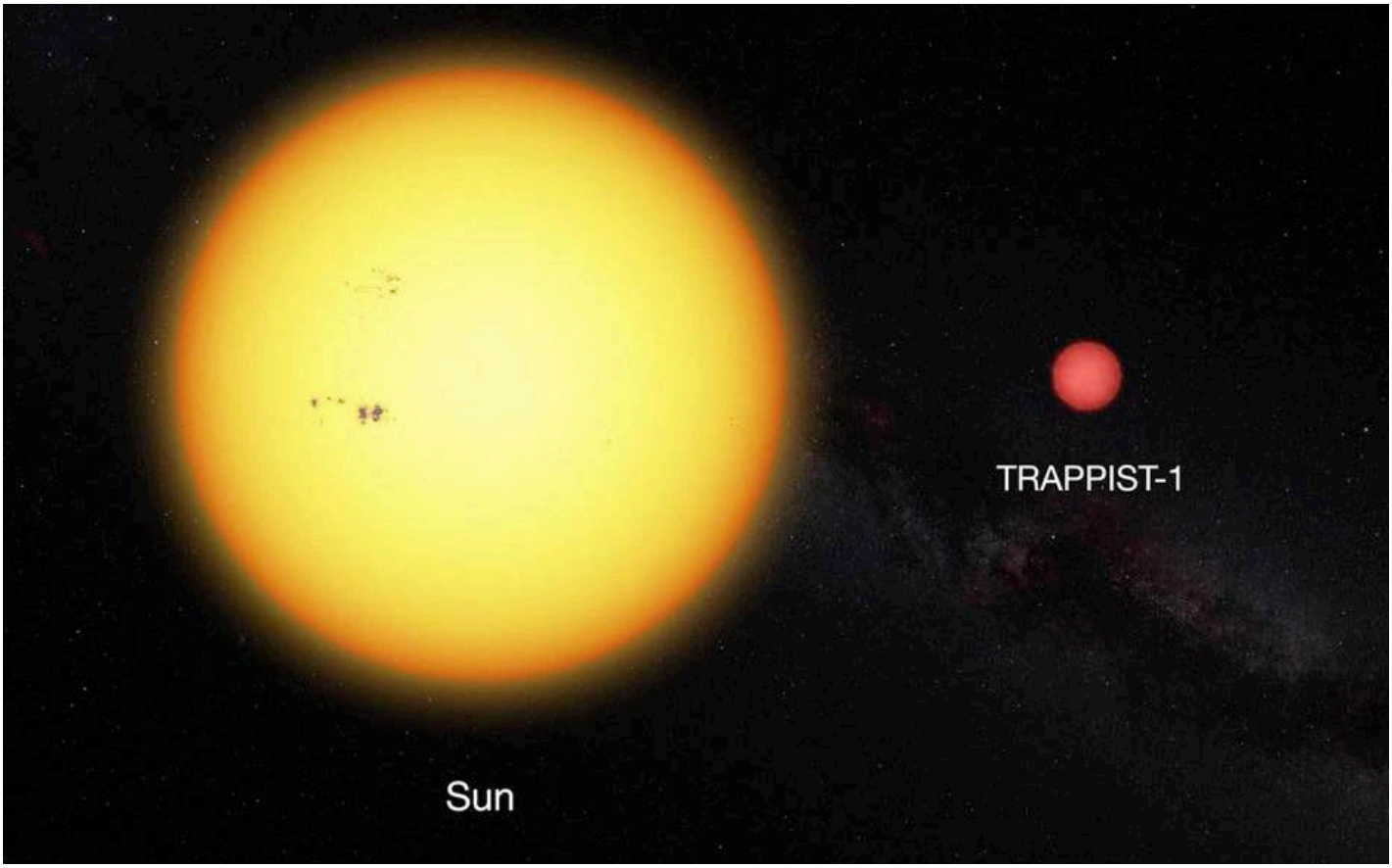
How the Search for Exoplanets is Spurring Creative Problem-Solving and Innovation

BY RACHEL ROCK

Scientists have discovered a new method of measuring the mass of exoplanets by using light.

(Photo Credit: C. Daniloff/MIT, J. deWit)

Earth. A temperate planet third from the Sun and most remarkably, the only planet in the universe that harbors life. Scratch that. The only planet that we know harbors life. Stars speckle the night sky like dew drops, their sweet luminescence but a tantalizing mystery. We have no idea what secret worlds may bask in their light, but we may be about to find out thanks to a research group headed by astrophysicist Michael Gillion. Gillon's TRAnsiting Planets and PlanetesImals Small Telescope (TRAPPIST) project has already revealed seven Earth-sized, temperate planets orbiting a dwarf star. Yet this is only the beginning. The team's Search for habitable Planets EClipsing Ultra-cOOl Stars project, or SPECULOOS, will use innovative technology and insight in order to offer us an invaluable glimpse into the darkness.



Of the thousands of stars speckling the black canvas above us, most are far smaller and dimmer than the sun. These are the stars Gillon's team is targeting. And looking for these little stars makes a very large amount of sense. As Julien de Wit, an MIT alum (PhD '14, XII) who collaborates with Gillon on the TRAPPIST and SPECULOOS projects, explained, "We tend to be geocentric, looking for Earth-twin systems, but, studying such systems in great depth will have to wait until the next generation. It is important that we do study systems in great depth with upcoming observatories, which is why it makes sense to look for planets around a small star. The signal of a planet in transit relates directly to the planet-to-star area ratio. Thus, if you have a star ten times smaller than

Above: The TRAPPIST-1 dwarf star is much smaller and more red in color compared to the Sun.
(Photo Credit: ESO)
Right: The Europa telescope searches the night sky for exoplanets.
(Photo Credit: Patrick Severin)
Opposite: This is one of the first images taken by the SPECULOOS Europa Telescope of the M83 Galaxy on March 17, 2017.
(Photo Credit: European Research Council)

Facilities like the James Webb Space Telescope will allow scientists to probe earth-like exoplanets.

(Photo Credit: James Vaughan)

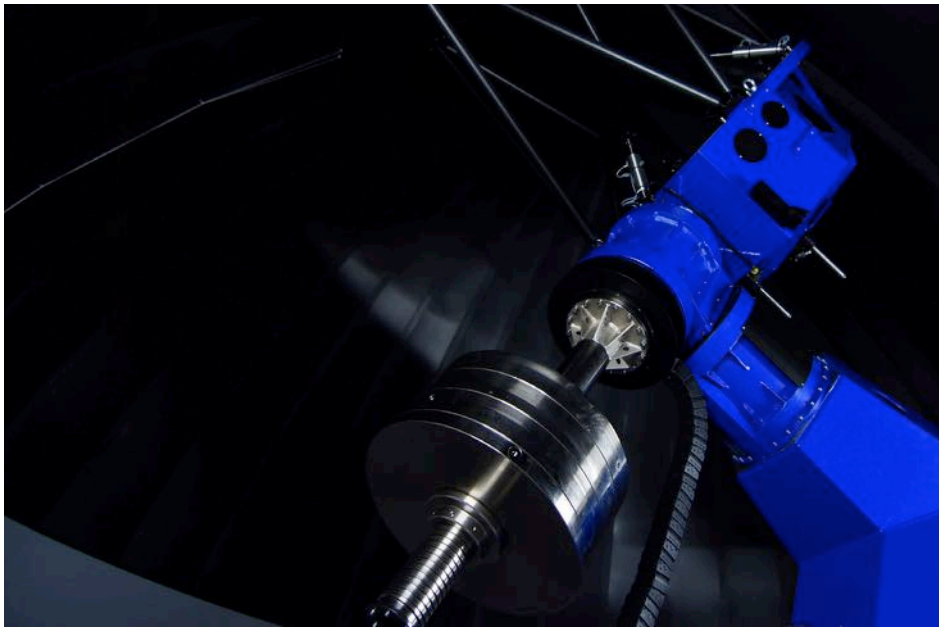
the sun, the signal of a planet will be about a hundred times larger than what it would be for the sun."

This clever strategy paid off—big time. In September 2015, the TRAPPIST Telescope hit upon something around TRAPPIST-1, an ultra-cool dwarf star a mere 40 light years from our solar system. Three temperate Earth-sized planets were announced on May 2, 2016. May 4, 2016, marked another big payoff: NASA's Hubble Space Telescope made the first spectroscopic measurements of two innermost planets of the TRAPPIST-1 system. Although these measurements were preliminary studies, they are the first steps towards searching for signs of habitability and life around the planets. Yet, next to the thrilling possibility of finding signs of life around TRAPPIST-1, the system will also help us better understand terrestrial planets as the seven that were found (which is three more than our system hosts, and in very different conditions) will be studied in great depth. De Wit said he is eagerly awaiting these discoveries, "I'll be excited with whatever we find because whatever we find should be different—on some level—from what we expect. And every time we see something different, it can help us to revise our perspective on it—and ideally reflect upon ourselves as well, so I'll be excited whatever we find."

But the journey may easily prove more important than the destination itself. Think NASA. The dream of space travel may not have landed us colonies on Mars but certainly has culminated in a myriad of life-improving discoveries: Advancing artificial muscle systems for extravehicular and robotic space activities led to the development of artificial limbs; NASA's aim to build a solar-powered aircraft capable of operating via remote at high altitudes

led to the creation of the silicon solar panels used by many energy-conscious home owners; the need to maintain the cleanliness of water brought to space resulted in modern water filters. From easy-bake ovens to enriched baby food, the list goes on and on. Yet all these discoveries were predictable because when brilliant minds come together in unexpected ways, brilliant and unexpected discoveries result. Since the investigation of these planets requires the galvanization of people from all fields, we very well may see some interesting developments not just out in space but also within our own lives.

With such immediate benefits and great potential, it is exciting that the search for exoplanets will be intensifying. As de Wit said, "We've already initiated a worldwide effort that ranges from x-rays to radio waves to search for signs of atmospheres and magnetic fields. We are now even directly in touch with SETI management. There's so much data to be gathered, so many channels to use in order to study this system." And SPECULOOS will help us track down even more systems like this. Soon to boast four telescopes in the Southern Hemisphere, and potentially one in MIT if de Wit can garner enough support (he has launched a fund-raising campaign at MIT to finance the acquisition of the SPECULOOS telescope for the Northern Hemisphere and to bring MIT on board of the SPECULOOS consortium as sole US partner), the project represents a photometric survey optimized for detecting Earth-sized planets transiting the nearest Southern ultra-cool stars. This will facilitate the discovery of more systems harboring potential similar to TRAPPIST-1.



The Europa telescope is the first of four telescopes to be built to find exoplanets.

(Photo Credit: J. de Wit)

Michael Gillon, Julien de Wit and collaborators are dedicated to their search for habitable exoplanets.

(Photo Credit: J. de Wit)

And this is but the beginning. The search for exoplanets is an enticing prospect in itself as these planets harbor the potential for life and new discoveries in this regard may spark a paradigm shift. Yet, research done in order to tease out these gems from the murky darkness shall likely prove invaluable in its own right. As Julien so aptly concluded, "Now, this is what we need to dream again."▪

Interview with MIT Postdoctoral Associate Julien de Wit:

Bettering the Earth by Challenging Status-Quos, from Planetary Sciences to the Baby Monitor Industry

BY RACHEL ROCK

Julien de Wit (PhD '14, XII) is a Postdoctoral Associate at MIT and member of the TRAPPIST[1] team whose SPECULOOS[2] project seeks to identify terrestrial planets that eclipse small, cool stars. In the prototype phase of the project, the team recently discovered seven Earth-sized, temperate planets orbiting around a white dwarf star known as TRAPPIST-1 (www.trappist.one). Such planets outside our solar system, known as exoplanets, harbor vast potential. Julien has helped the team learn more about these planets and search for others. He has also launched a fund-raising campaign at MIT to finance the acquisition of SPECULOOS telescopes for the Northern Hemisphere and to bring MIT on board the SPECULOOS consortium as sole US partner.

SPECULOOS will soon boast 4 telescopes—all in the Southern Hemisphere, with the very first having been installed in Chile only recently.

What was it that drove you towards exoplanetary science?

When I came for the first time to MIT as a visiting scholar to help support the design of MIT Professor Sara Seager's cubesat ExoplanetSat[3], she introduced me to the idea that soon we will have the opportunity to study in great depth the atmospheres of worlds beyond the edge of our solar system. The idea of studying the atmospheres of other worlds, assessing their habitability and possibly find signs of life there got me hooked, so I dove into this new field. One could say that I stumbled into it. As I was coming with fresh eyes—and the field itself was relatively new—there was (and still is) a lot to be done, a lot of room for new techniques to be developed, new insights to be extracted from unprecedented data sets, i.e. for creative exploration.

The first project I did aimed to find out what we could learn about distant worlds using a technique called transmission spectroscopy (http://webbtelescope.org/video/859/science). I went back to the first principle of relative transfer in order to look at what are the actual pieces of information you can get through a transmission spectrum, which basically relates how the light coming from a star—when a planet is in front of it—passes through the planet's atmosphere and is affected by it. For an analogy, picture how the color of the light passing through a glass will change depending on its content (e.g., water, orange juice, wine), i.e. the composition of the medium through which the light is transmitted. It's really important to define what you can actually extract, especially to know if you will actually be able to assess the habitability of exoplanets.

I was also wondering about the technique you developed to map these distant worlds. These exoplanetary systems are so far off that the only thing that you can see is one bright dot where all the light coming from the planet, the star, is condensed, meaning that you can't even spatially resolve the star. And yet, you have found a way to extract spatial information about the planets.

I agree that this technique, known as eclipse mapping, is pretty cool as it allows us to map a planet that is way smaller and fainter than its host star, which we could not normally map (a nice example of the true beauty of data science!). Back in Belgium in 2011, I was working with Michael Gillon[4] on a large set of observations of the hot Jupiter HD189733b acquired with the Spitzer Space Telescope and realized that there was something strange: when the planet was passing behind its star and then reappearing behind it, our models could not properly fit the respective decrease and then increase in flux. The reason was that the community used to simulate the planets as uniformly bright disks while planets are not; they have bright (i.e., warm) and faint (i.e., cold) regions over their globes. Using a simple, uniformly-bright disk as a model was fine before, but it became an issue as the quality of our data increased. Capitalizing on the fact that the planet was basically scanned by the stellar limb in two different directions as it disappeared and reappeared from behind it, we developed a technique creating

a 2D map of the planet. And yet, this was just the beginning because if you observe such a signal at different wavelengths, you are probing different optical depths and, hence, different pressure levels, which allows you to work towards a 3D map of the exoplanet atmosphere. Hence, you can study complex 3D structures in the atmosphere of other worlds while, once again, you're not even able to resolve the host star. It's a lot of data science, which I like. And new facilities such as JWST[5] will allow us to dive deeper.

On that note, you have launched a fund-raising campaign at MIT to finance the acquisition of the SPECULOOS telescope for the Northern Hemisphere and to bring MIT on board of the SPECULOOS consortium as the sole US partner—what do you feel makes this telescopes so spectacular?

You know that I'm here in Paranal, Chile. It was the official first light yesterday for the SPECULOOS telescope[6]. And, yes, this telescope is remarkable, but it also looks super cool—it looks like a big crane (the bird) ready to fish for planets. The quality of the optics is exceptional. Michael really wanted to focus on the smallest stars in the galaxy (which are also the most frequent), which really made sense: We tend to be geocentric, looking for Earth-twin systems, but, being optimistic, it will be at least 30 years before we can study these Earth-twin systems in depth. It is important that we do study systems in great depth with upcoming observatories, which is why it makes sense to look for planets around a small star. The signal of a planet in transit relates directly to the planet-to-star area ratio. Thus, if you have a star ten times smaller than the sun and have a planet about the size of Earth in front of it, the signal will be about a hundred times larger than what it would be for the sun. Yet, no one had really dared to push for technology to go down and search for planets around such small and cold stars, which are called UCDs[7]. We really can't wait to see what SPECULOOS will find. The beauty is that if you locate Earth-sized planets around these stars, you can probe them with upcoming facilities, such as JWST, which is the most important part of this venture: It is actually providing us with targets that we can study and search for signs of habitability within the next decade and hopefully signs of life within the next generation.

Oh wow.

Wow indeed. But we are not waiting for these observatories; we've already initiated a worldwide effort that ranges from x-rays to radio waves to search for signs of atmospheres and magnetic fields. We are now even directly in touch with SETI[8] management! There's so much data to be gathered, so many channels to use in order to study this system, it really is just the beginning…

So this really is an intersection of every field.

Yeah--and that's why it's so cool. We need everyone from quantum physicists to biologists, biochemists, geophysicists, atmospheric scientists, engineers, and oceanographers. Finding planets, analyzing them, and learning about their potential habitats remotely requires a wide range of expertise, which is great because this will push our field towards a more community-based effort. On the other end, it's great to see so many individuals connected to providing us with different perspective of planets, evolution, life and habitats, which I see as the key benefit of this field. The new vantage points that we will get with this research will be shared all along through various fields and continents, which is good. Now, this is what we need to dream again.

With respect to life, what do you think we may find and what discovery would excite you most?

I'll be excited with whatever we find because whatever we find should be different--on some level--from what we expect. And every time we see something different, it can help us to revise our perspective on it—and ideally reflect upon ourselves as well, so I'll be excited whatever we find. I tend to believe there shall be life. To me, it seems that life is a natural process: It emerges, it evolves, and it can make the best of any circumstance. I assume that we will first find signs of biomass, by which I mean microorganisms. What's interesting is that the definition of biosignatures makes it more difficult for us to reveal the signs of non-intelligent biomass but if you find something like CFCs, pheromones, or another complex molecule, then you would know that there is something beyond microorganisms. To be honest, I don't know what we're going to find first, but I don't think it will matter much as the outcome which will be the same:

paradigm-shifting in any case.

Out of this world—literally. But back to Earth. What are your other interests?

Something that will surprise you—for sure—is that along with Stephen Messenger (a friend and MIT Alumni), we started a company for baby monitors, Morpheus LLC. This baby monitor is a new type of monitor that helps parents have both a greater quantity and quality of sleep—so it is just another way of trying to make people's life a bit nicer to allow them to move beyond the "survival mode" induced by continuously increasing level of stresses. The idea is very simple: Most baby monitors pick up sounds and then broadcast the noise in the parents' room, thereby awaking both parents in a rough manner. What we are moving towards is a monitor that uses vibration, via a wristband, to wake one parent smoothly and quietly, so the other one can keep sleeping. The monitor allows parents to choose who is on duty and when and if one parent does not wake up, the other will be awoken.

Is there any advice that you would like to give to future students?

The most important for incoming students is to keep on following their initial passions while being open to everything that MIT has to offer. Doing so genuinely is the best way to become an expert while enjoying one's journey. This will require facing the fears that naturally come with joining a place with so much potential (both in terms of research topics and individuals). This will be overwhelming at times: Being "simply average", so many—too many—exciting opportunities, an apparently infinite intellectual space… Handling this change of circumstance will require a whole new level of self-love and self-confidence, both of which will also allow for deep connection to peers who will surely act as catalyzers for growths in many dimensions of their life. Self-love and self-confidence are the basics of a successful MIT 101, the key to fully benefit from the countless opportunities that await here.

Notes

[1] TRAnsiting Planets and PlanetesImals Small Telescope

[2] Search for habital Planets EClipsing ULtra-cOOl Stars

[3] A Cubestat is a mineature satellite designed for space research that aligns to standards set forth by California Polytechnic State University, San Luis Obispo and Stanford University's Space Systems Development Lab in 1999

[4] Michael Gillon is principle investigator of the TRAPPIST-1 team and SPECULOOS

[5] James Webb Space TelescopeFare nov

[6] For more on Julien's fund-raising campaign at MIT to finance the acquisition of the SPECULOOS telescope for the Northern Hemisphere and to bring MIT on board of the SPECULOOS consortium as sole US partner, see https://eapsweb.mit.edu/giving-alumni/new-worlds-new-priorities

[7] Ultra-Cool Dwarves

[8] Search for Extraterrestrial Intelligence, or SETI is a nonprofit research organization that seeks to investigate the nature of life in the universe while promoting STEM goals (https://www.seti.org/seti-institute/a-seti-signal)

MURJ Reports

A New Perspective Toward the Design of Creative Cities

Kenneth K.A. Acquah[1], Dr. Arnaud Grignard[2], Prof. Kent Larson[2]

[1]Student Contributor, Class of 2020, Department of Computer Science and Department of Economics, Massachusetts Institute of Technology (MIT), Cambridge, MA 02139, USA

[2]Changing Places research group, Department of Media Arts and Sciences, Massachusetts Institute of Technology (MIT), Cambridge, MA 02139, USA

Urban Planning is a social engineering field central to the economic, creative, and social growth of our increasingly urbanized society. Unlike most engineering fields, the design of efficient and collaborative cities is not an activity that allows much room for failure. The ability to successfully and accurately model such a task could provide designers with essential insight into what urban designs produce prosperous city configurations. In this paper we discuss how we attempt to solve that problem through the design of a GAMA (GIS Agent-Based Modelling Application) model that takes in input from The Changing Places Lab's Tangible Interactive Matrix (a tool in which one can input configurations into an agent-based model by placing Lego constructions on a square grid). To test the validity of our model we analyzed the results it outputs due to a variety of input configurations. We found that our model was mostly successful in showing designers which configurations provide a welcoming environment for economic and creative growth; a discovery that could greatly improve the means by which urban planners approach implementing design concepts.

1. INTRODUCTION

In 1988, David Yencken revolutionized the fields of urban planning and regional economics when he introduced the concept of the "Creative City," setting off the spark that burst into fiery global movement. The goal of creative city design is to forge an organizational structure that inspires ingenuity and acceptance, providing fertile soil for the steady growth of an innovative economy. The infrastructure that fosters a creative city includes elements such as efficient transportation, mixed-used development, a skilled and educated labor force, and a tolerant populace. These elements, according to proponents of the concept, are responsible for attracting and rearing the creative talent that promotes innovation within a city (Florida, 2002).

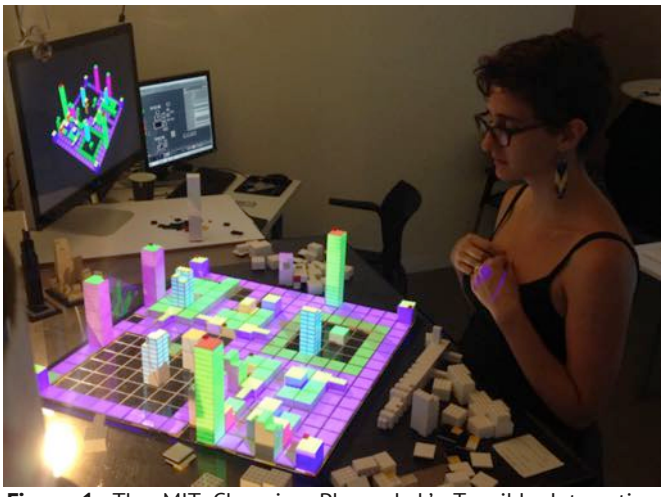


Figure 1: The MIT Changing Places Lab's Tangible Interactive Matrix, the device uses a set of cameras to upload the current configuration of the matrix to a hosted web server, so physical manipulations and designs can be transferred online, where models can be run on specific configurations.

For decades, people studying the urban planning have wondered, what exact configurations make for a creative city? How do creative cities grow and propser? What effects do the elements of "Creative Cities" have on their general population? In addition, practicing city planners have quite a vested interest in understanding how to improve the "creativity" of developed areas. These questions and problems can be solved by utilizing the potential for tactile experimentation unleashed by the MIT Changing Places Laboratory's "Tangible Interactive Matrix" (TIM), as well as agent-based modelling to build an interactive, real-time, didactic model of the creativity of a growing city and how it changes over time in response to a variety of factors. This paper outlines the design aspects and results of such a model as well as an analysis of the assistance the model provides towards understanding the planning of creative cities.

2. INSPIRATION

Our model draws inspiration from a number of sources, namely, two influential contemporary books on the rise of creative cities, ("The Creative Class" by Richard Florida (2002), and the "Triumph of the City" by Edward Glaeser (2011))

and another similar implementation of this model in the NetLogo agent based modelling language. The following section outlines what exactly our model draws from these sources, in addition to elements that make our findings distinguishable from the findings of these sources.

2.1 The Theory of the "Creative City"

Both Florida and Glaeser provide a detailed account of creative city elements, based on their analysis of a variety of case studies of cities across America. Reading their personal theories of the infrastructure that affects city creativity provided a helpful starting point in deciding what specific elements of cities should be included as parameters and variables within our Creative City Model.

The infrastructure elements from the works of Glaeser and Florida that we decided to include in our Creative City Model were:

- **Green Spaces.** Areas such as parks and gardens that foster creativity through aesthetic beauty and open recreational space.
- **Universities and Public Schooling.** The addition of universities and public schooling attracts creative people who value education for themselves and their families, nurtures creativity in the city's younger population, and provides hotbeds for entrepreneurial and academic growth.
- **Business Friendly Economic Policies.** Cities with economic policies that promote the existence and growth of business attract businesses of all sizes, these businesses in turn attract members of the creative class to these cities.
- **Mixed-use Development.** It has been shown that mixed-used development, development that features interspersions of many types of infrastructure (such as commercial, residential, parking spaces, and green spaces), is much more conducive to the development of creative spaces than development that is more distinctly zoned and divided.
- **Diversity and Tolerance.** In general, creativity spawns from diversity: a mixture of culture, of disciplines, and of schools of thought enables the collaboration and fruition of novel ideas. Tolerance is a necessary trait in order for a city to attract and utilize the full power of diversity.
- **Social Capital.** The presence of interconnected social networks, within which citizens of different firms can innovate with each other and disseminate creative ideas promotes creative and economic development within cities.
- **Proximity.** Creative areas must be close together in order to mutually boost each other's creative value.

Rank	Metro	Creativity Index	Technology Index Rank	Talent Index Rank	Tolerance Index Rank
1	Boulder, CO	.981	10	5	9
2	San Francisco-Oakland-Fremont, CA	.970	3	16	17
3	Boston-Cambridge-Quincy, MA-NH	.968	9	9	20
4	Ann Arbor, MI	.961	25	10	10
4	Seattle-Tacoma-Bellevue, WA	.961	1	22	22
4	San Diego-Carlsbad-San Marcos, CA	.961	7	37	1
7	Corvallis, OR	.959	14	8	25
8	Durham, NC	.953	8	1	45
9	Washington-Arlington-Alexandria, DC-VA-MD-WV	.947	27	3	30
10	Trenton-Ewing, NJ	.945	44	6	13
11	Ithaca, NY	.937	61	4	6
12	San Jose-Sunnyvale-Santa Clara, CA	.933	2	2	71
13	Portland-Vancouver-Beaverton, OR-WA	.930	4	59	16
14	Worcester, MA	.922	30	40	18
15	Burlington-South Burlington, VT	.918	11	20	61
16	Hartford-West Hartford-East Hartford, CT	.916	42	14	37
16	Austin-Round Rock, TX	.916	5	54	34
18	Minneapolis-St. Paul-Bloomington, MN-WI	.915	17	23	53
19	Atlanta-Sandy Springs-Marietta, GA	.912	23	33	42
20	Tucson, AZ	.909	12	64	26

Figure 2: A table from Richard Florida's "The Rise of the Creative Class Revisited" (2012) displaying the Creativity Index of various cities. The Creativity Index is, according to Richard Florida, an overall measure of regional economic potential and is composed of three T's (Talent, Technology and Tolerance).

2.2 NetLogo Creative City Model

Our model aims to improve a model previously created in NetLogo by researchers at George Mason University, that was "designed as a tool for understanding the relationship between human creativity and urban development through transportation, social segregation and land-use regulation perspectives" (Overview, Design concepts, and Details (ODD) of the Creative City Model [ODD], 2014).

Fundamentally, the model uses a grid to represent areas of the city that residents can be affected by and interact with. The squares of the grid are various types, each of which interacts differently with the citizen agents in the model. Agents of the model move around until they are content with the square they occupy, which requires the square to have a level of diversity below a certain "Tolerance Threshold" as well as a rent that they can comfortably afford.

Our version of the model greatly simplified the NetLogo model to provide a more digestible analysis of Creative City design.

3. MODEL SPECIFICS

3.1 Land Use

Similar to the original NetLogo Model, the squares of the grid in our model are divided into four designated land use types. Each of these types interact differently with the residents of the city as well as the other squares nearby. The four types of land use are:

- **Green Spaces.** These squares encourage creativity in the areas around them to reflect the effects that Green Spaces are theorized to have on the creativity of a city. They are uninhabitable and can only become creative as a result of influence from their surrounding green and creative spaces.
- **Residential Spaces.** These squares are where resident agents of the city live. They can become creative if there are enough creative people inhabiting them.

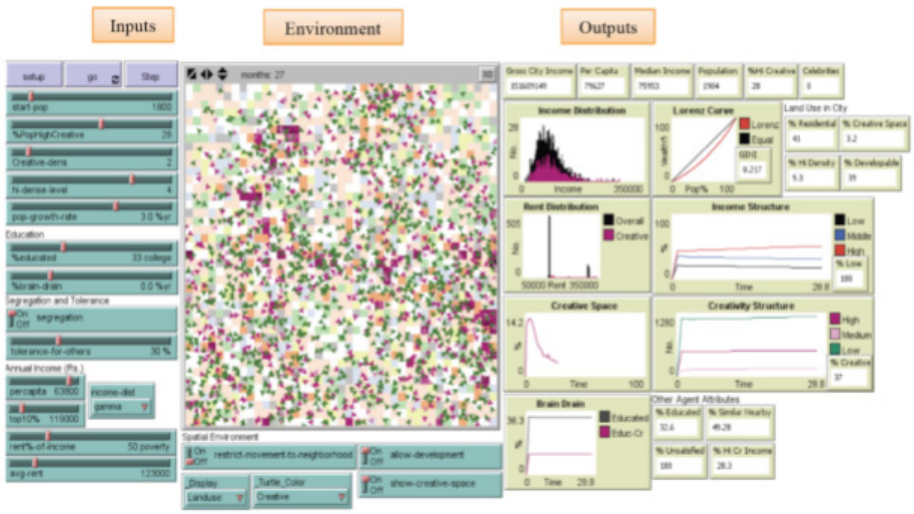


Figure 3: A screenshot of the NetLogo model from which our model draws inspiration.

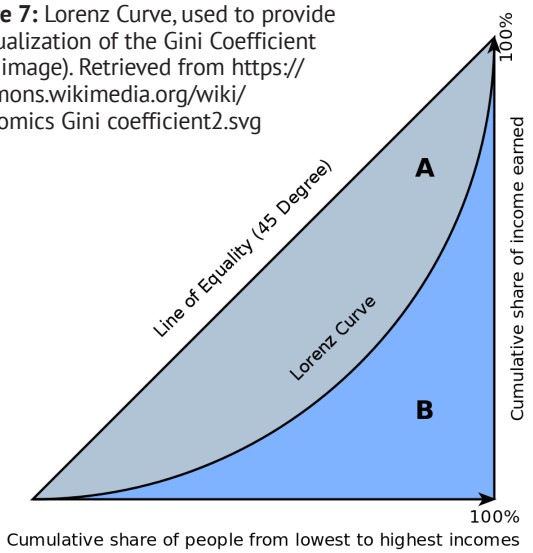
- **Commercial Spaces.** These squares are where resident agents of the city work and trade goods and services. They can only become creative as a result of influence of their surrounding green and creative spaces.
- **Undeveloped Land/Road and Parking Spaces.** The residents do not interact with these squares at all. They can only become creative as a result of the influence of their surrounding green and creative spaces.

3.2 Segregation Modeling

According to the literature we referenced throughout the construction of our model, tolerance for other types of people is a major aspect of supporting creativity.

This can be modeled with the classic Schelling Segregation Model, often used to represent the effects and perpetuation of segregation on a city. Our creative city model follows a similar set of rules: Initially, the residents are assigned to residential locations on the grid randomly, and all members of the city have a set tolerance for species of a different color in their area. When the percentage of species around them that are of a different color is greater than the tolerance of residents in the city, they migrate to another random location until they are satisfied with their surroundings.

Figure 7: Lorenz Curve, used to provide a visualization of the Gini Coefficient (SVG image). Retrieved from https://commons.wikimedia.org/wiki/Economics Gini coefficient2.svg



3.3 Income Model

The creativity of residents of a city has been observed to have a significant effect on the income structure of the city. One fear held by many theorists about "The Rise of the Creative Class" is its amelioration of urban income equality. To promote our model's goal of providing designers and researchers a holistic view of the development of Creative Cities, we included an income model that can be monitored and analyzed to better understand the phenomena.

Within our model, the starting income of the city's residents is modelled with a gamma income distribution, a distribution chosen because it has been shown to provide accurate analysis of income distributions in western countries. As the events of the model proceed, the income distribution alters, resulting in an increase in income inequality. The income inequality of a city can be quantitatively measured by the city's Gini Coefficient which is equal to A/(A+B) of the labeled curve in figure 7 (Morgan, 1962).

3.4 Population Growth, Education, and Creativity

The model's rules for population growth, education, and creativity are all rather straightforward.

- The population growth of the city is the percent increase in residents in the city every year
- The percent education of the city is the percent of the city that is educated at any given time
- The percent creative educated of the city is the percent of the city that is both educated and creative.
- All creative residents are also educated.
- **Brain Drain** is another parameter that can be used to indicate how many creative members of the city leave the city per year. Brain drain is a real problem that many struggling cities face year after year.

The percent of the population is proportional to the percent of the population that is educated to demonstrate the important fact that an educated populace has been proven time and time again to be a necessary condition of a sustainable creative populace.

3.5 High Creative Value Land Usage

A very important aspect of our creative city model is the way in which it represents the utilization of land within cities as "creative spaces" or spaces that spawn, as well as attract, high creative activity. In addition to the presence of creative spaces, certain spaces are listed as "high creative spaces". High creative spaces follow the same rules as other creative spaces, but the effect that they have on their residents, as well as the

Figure 5: The four land use types included in our model.

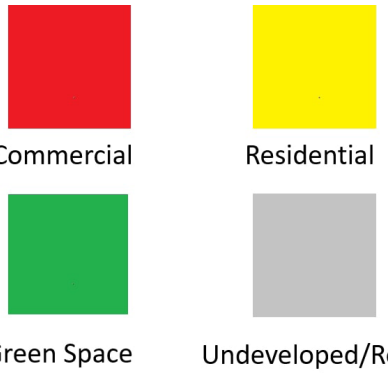


Figure 6: The representations of the different resident types within our model.

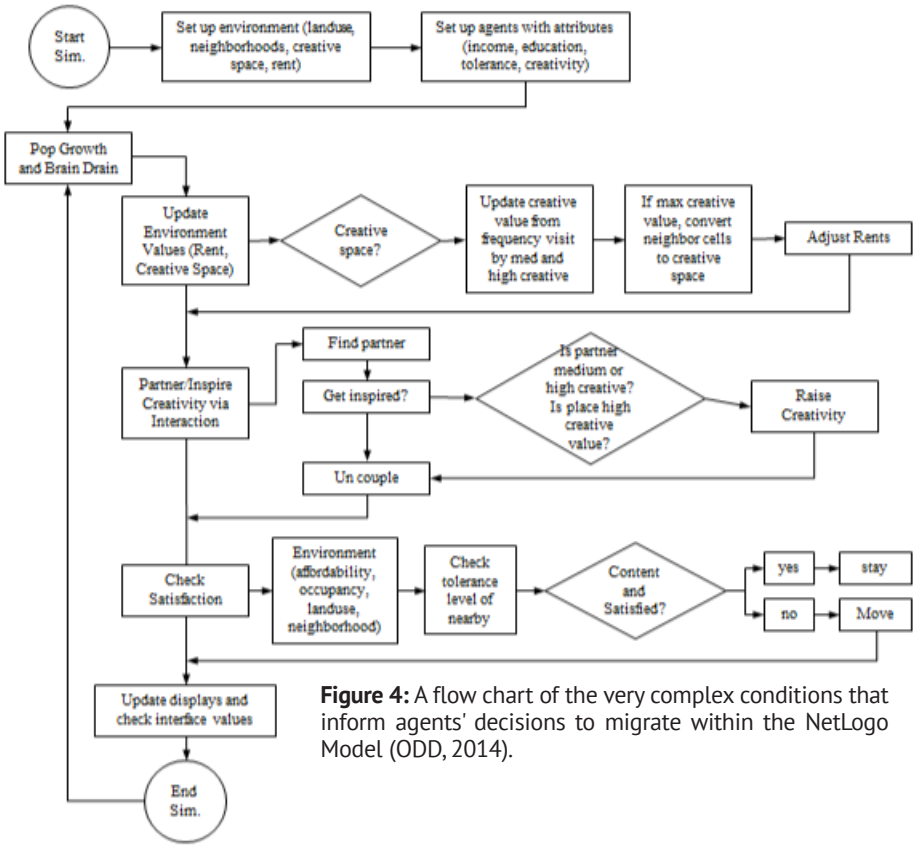
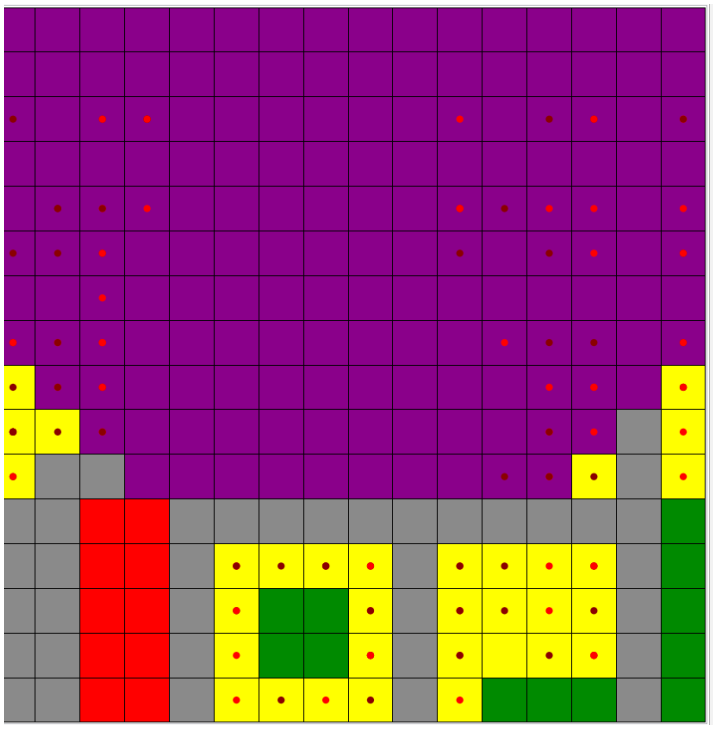


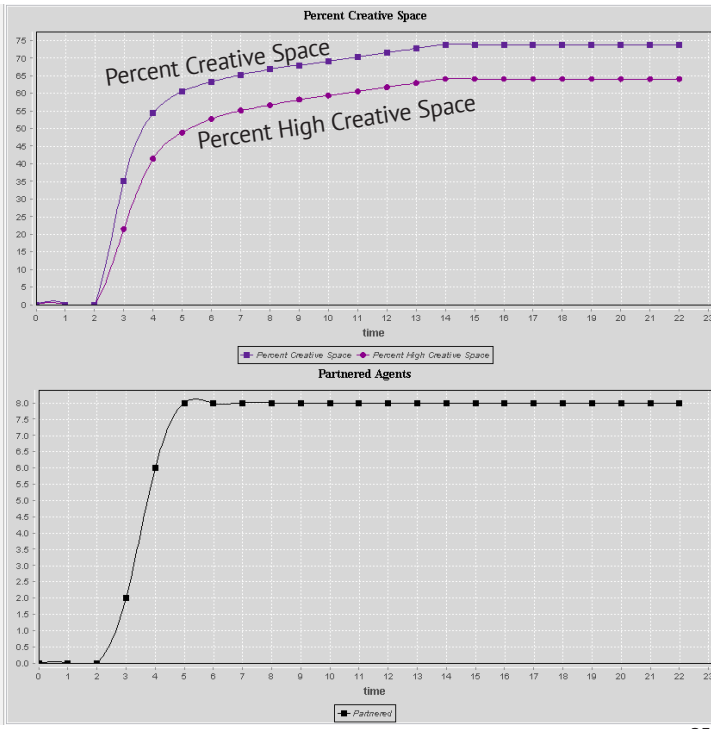
Figure 4: A flow chart of the very complex conditions that inform agents' decisions to migrate within the NetLogo Model (ODD, 2014).

surrounding squares in the city is amplified. The transformation of regular squares into creative spaces and highly creative spaces follows the rules below:

- Every time a creative member of the creative class lands on a residential patch, either because their previous neighborhood had too many residents that were dissimilar to them, or because of trivial random movements that happen often within residents of a city, the creative patch gains 5 creativity points.
- When a residential patch has more than 50 creativity points, it is turned purple to represent that it has become a creative patch when a residential patch has more than 100 creativ-

(Below) Figure 8: A depiction of the transformation of a city from uninspired to creative, accompanied by a graph that records the percentage of the land that has been transformed into creative space. To the right of this graph is a plot of the number of residents of the city have partnered up and have made an attempt at an entrepreneurial venture.





ity points, it is turned dark purple to represent that it has become a highly creative patch.
- When a residential patch becomes highly creative, the surrounding patches receive 27 creativity points.
- Direct proximity to green spaces results in patches receiving 20 creativity points.

3.6 Partnership and Entrepreneurship

One of the hallmarks of a creative city is a burgeoning entrepreneurial community. It is from this community that innovation, wealth, and economic growth arise and self-perpetuate. However, entrepreneurship does not spawn in a vacuum. It must be crafted in an environment of higher education institutions, social capital between both creative and non-creative residents, and an openness to collaborate between dissimilar groups of people. The rules of our model that are meant to represent the cultivation of entrepreneurship reflect this understanding of the elements necessary for its growth. The rules are as follows:

- A certain percent of residents every month choose to pursue business and entrepreneurial partnership with other members of the creative class.
- There is a set probability that two members of the same group will create something if they meet on a creative patch. For members of different groups, this probability is multiplied by the tolerance of the members of the city.
- Creative people can either partner with non-creative people in creative spaces and inspire creativity or start a business with other creative people.

4. RESULTS OF MODEL RUNS

Once we had completed the model, we ran it on a variety of configurations of the Tangible Interactive Matrix. These configurations were built to represent both conventionally good and bad designs of cities. The first of the four designs was based on characteristics of well-designed cities: mixed-development, which features a healthy mix of residential spaces, commercial spaces, and green spaces. The second was based on divided development: it was constructed very similarly to the mixed development configuration, but with a clear distinction between office areas, green spaces, and residential areas. The last two designs were both based on two common causes of urban sprawl: the third represents the effects of a city that is build densely in its center and increasingly sparse as one radiates out, the fourth represents the effects of a city that features a lot of low density commercial development, resulting in a need for a large amount of street space and parking lots, inhibiting residential development. The results of running the model on these four configurations confirms many contemporary understandings of how to most efficiently construct an urban neighborhood.

4.1 Mixed-Use Development

The Mixed-Use Development configuration was designed to reflect the modern city layouts that utilize mixed-use zoning, a zoning structure that blends a variety of land uses together in one area. Mixed-Use development is thought to provide many tangible benefits to cities around the world, including land-use synergy (a term to describe the support that different kinds of land-use provide each other) increased transit opportunities, affordable housing, and a more substantial sense of community (Beyer, n.d.). In our model specifically, divided development allows creativity to flow more frequently from residents to their surrounding businesses and allows for both residential and commercial squares to be influenced by nearby green spaces.

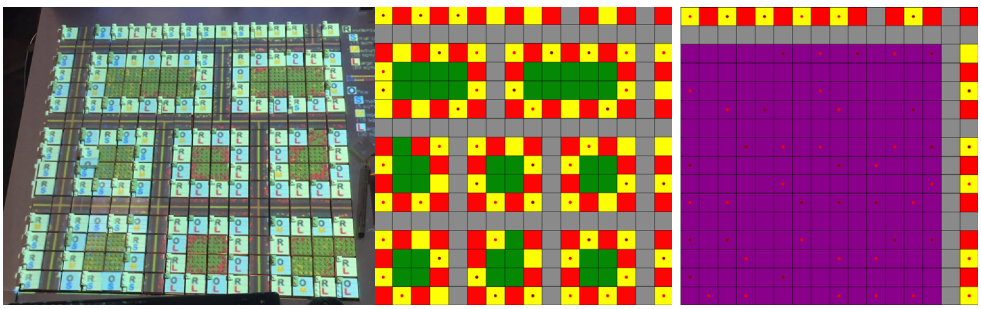
These attributes (analogously to the benefits of land-use synergy, accessibility of transit opportunities, and the sense of community of mixed-use development in real cities) result in our model very quickly becoming almost entirely creative, mirroring the documented success of the cities that this configuration aims to model. One glaring drawback of the Mixed-Use Development configuration is a very high Gini Coefficient.

4.2 Separate-Use Development

The Separate-Use Development configuration is built to model the creative growth of cities that have equal parts residential and commercial areas, but have these areas strictly divided across the city. As a result of increases in industrialization as well as the invention of the skyscraper, separate-use development was the primary development strategy for cities throughout the twentieth century; only recently are urban planners abandoning the style for the more sensible, more flexible mixed-use zoning. While running our model on this configuration, we were intrigued to learn that separate-use zoning also resulted in our model city becoming mostly creative, however much slower than mixed-use configuration. Even though the separate-use configuration is by no means "a perfect city configuration", the presence of a variety of elements that enable creativity, however segregated, seems to be enough to achieve economic growth. The division between the residential and commercial areas of the city, however, spawns divisions between the commercial activity of the residents in the city, slowing entrepreneurial and creative growth for most members of the city.

When looking at the results of the model, it can be seen that the model produced positive results in this configuration, besides the timing issue (this configuration takes about 300 months to become fully

Figure 9: Initial layout of mixed-use development configuration, at left and center. At right: layout of mixed-use development configuration after 20 months.



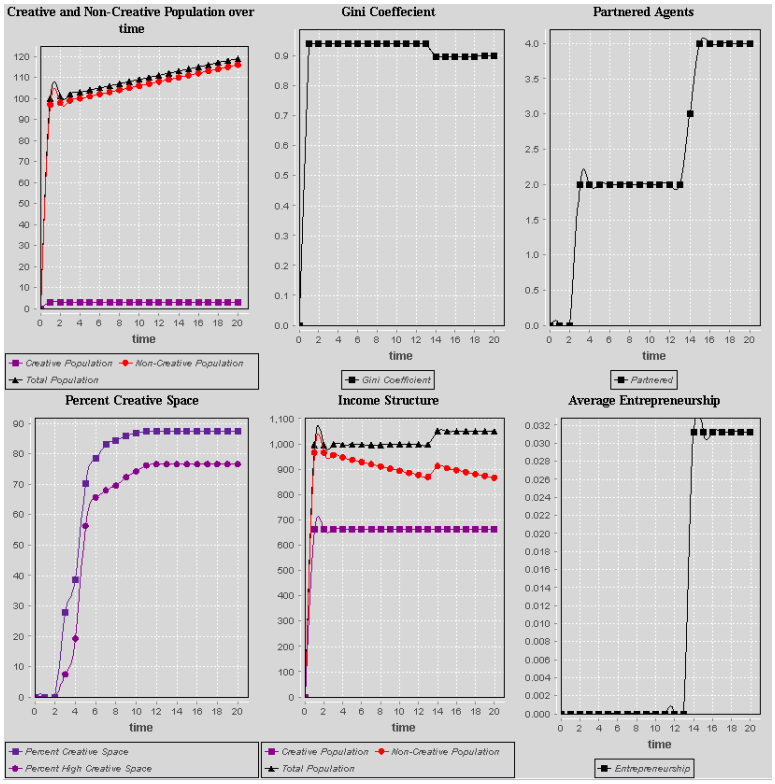


Figure 10: Time series of metrics taken for mixed-use development configuration after 20 months.

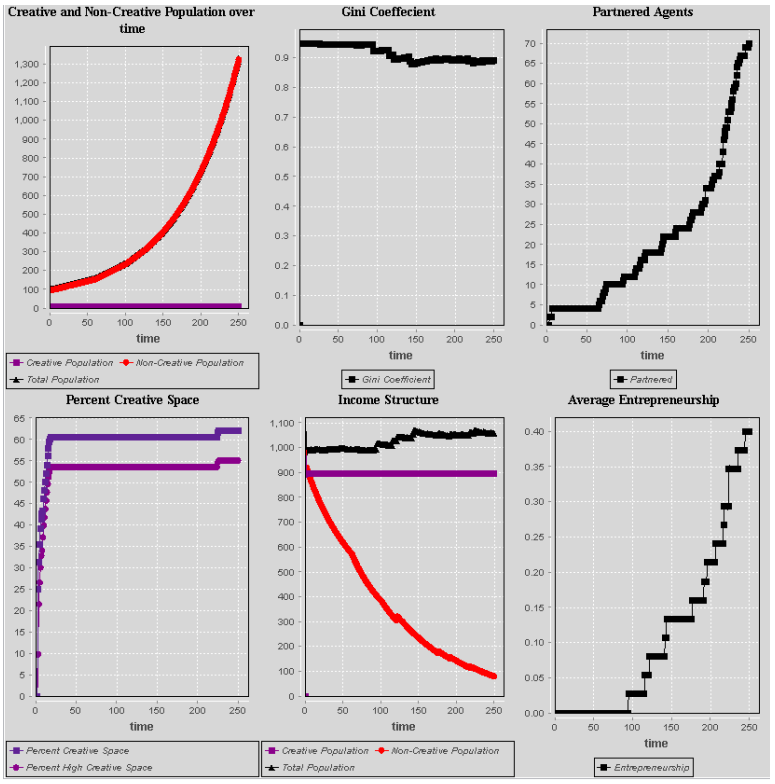


Figure 12: Time series of metrics taken for separate-use development configuration after 250 months.

creative), and the drawback of a high Gini Coefficient (showing that our city faces serious issues with income inequality).

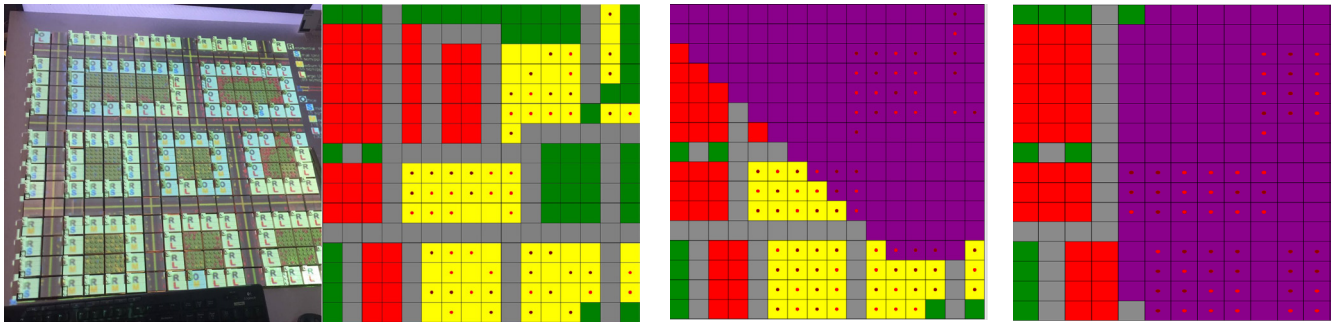
4.3 Commercial Urban Sprawl

The next two configurations were built to represent urban sprawl, or the low-density geographic expansion of urban populations. Urban Sprawl is a highly politicized topic in the field urban planning and mostly spoken of with a negative connotation. The phenomena has been found to have a slew of detrimental effects on the environments, health, infrastructure budgets, and social capital of societies. In the context of our model, urban sprawl results in little communication between creative residents and fails to create an atmosphere for flourishing entrepreneurship (Chin, 2002). In addition, our urban sprawl configuration has few squares of green spaces placed in its center, reflecting the common lack of green space in cities that suffer from urban sprawl. The first urban sprawl configuration, commercial urban sprawl, represents the effects of urban sprawl that arises out of large amounts low-density commercial development, such as strip-malls and large single story department stores. These businesses require large amounts of land area, for their buildings and for their customers to park their cars, inhibiting residential development. Even though this configuration eventually became fully creative after the influx of a creative population eventually enabled it to (after about month 200), at lower populations, it entirely failed to provide a nurturing environment for creative activity, emphasizing its failure as an urban planning structure. This failure can be seen in the grid on the right in figure 13.

4.4 Central Urban Sprawl

Much like Commercial Urban Sprawl, Central Urban Sprawl is an urban planning concept characterized by low density development and a lack of foresight when designing zoning. Central Urban Sprawl has a few key differences from Commercial Urban Sprawl. The former does not result from planning that favors high

Figure 11: At left and second from left: initial layout of separate-use development configuration. Second from right: separate-use development configuration after 250 months. At right: separate-use development configuration after 300 months.



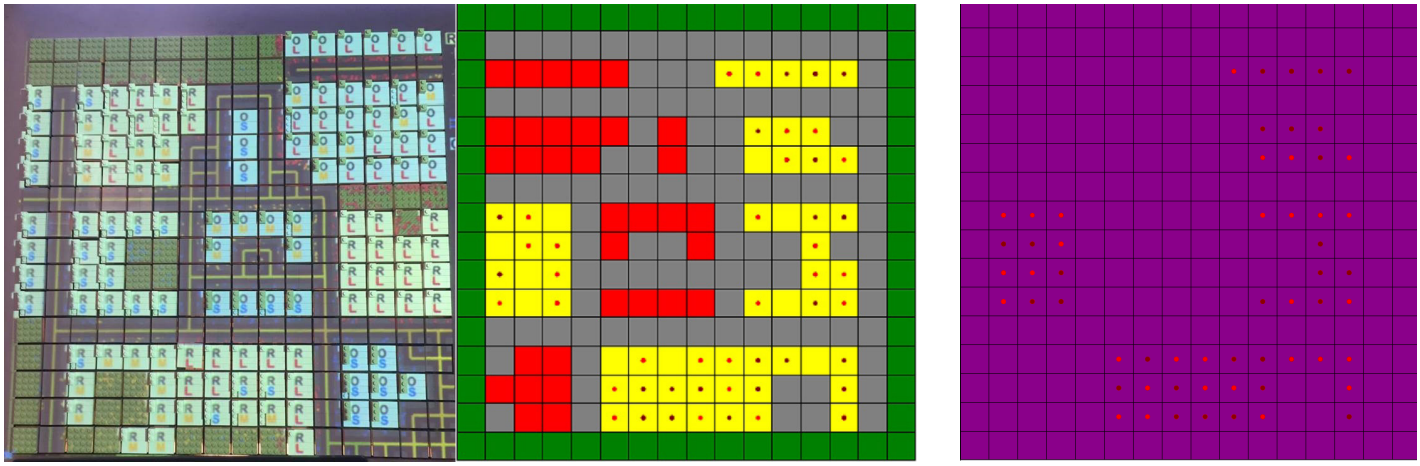


Figure 13: Left and center: initial layout of commercial urban sprawl configuration. At right: layout of commercial urban sprawl configuration after 216 months.

commercial businesses that require large amounts of land, but rather, results from a lack of planning altogether. Cities that are diagnosed with Central Urban Sprawl are those with a central commercial area surrounded with low-density residential areas and agricultural space. This class of urban sprawl suffers from many of the same detrimental effects as Commercial Urban Sprawl, but surprisingly does not entirely fail to provide an environment for an economically successful creative city, at least according to our model. There are many reasons this could be the case. One possible explanation would be that, as one can see in Figure 20, we designed all of our configurations to experiment with only one factor, and while our Central Urban Sprawl configuration features a sharp divide between its residential and commercial areas, we allowed for it to be heavily populated with green space, which provides a significant boost to the cities' creativity, according to our model. However, even though this configuration is successful in the formation of a creative city, it is important to realize that this is not the optimal configuration for cultivating such a city; this configuration does not completely become creative, unlike the more optimal mixed-use development configuration.

5. CONCLUSION

Agent-based modelling has been proven time and time again to be a helpful resource to people interested in gaining a further understanding for economic phenomena in the real world. Utilizing the creative city model, we were able to test contemporary theories about various city environments and their effects on the creative and economic development of their corresponding residential and commercial ecosystems. While some results, were as expected, (the Mixed-Use Development configuration very quickly yielded a highly creative city, the Central Urban Sprawl configuration was never able to become fully creative), others were quite surprising (both the Separate-Use development and the Commercial Urban Sprawl configuration eventually became mostly creative).

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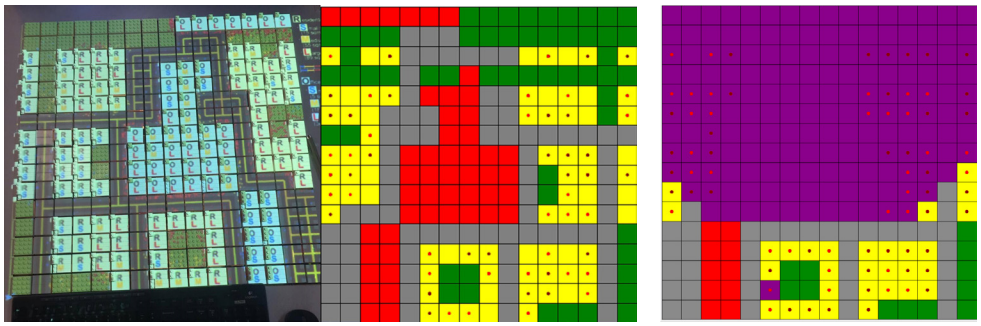
Figure 15: At left and center: initial layout of central urban sprawl configuration. At right: layout of central urban sprawl configuration after 216 months.



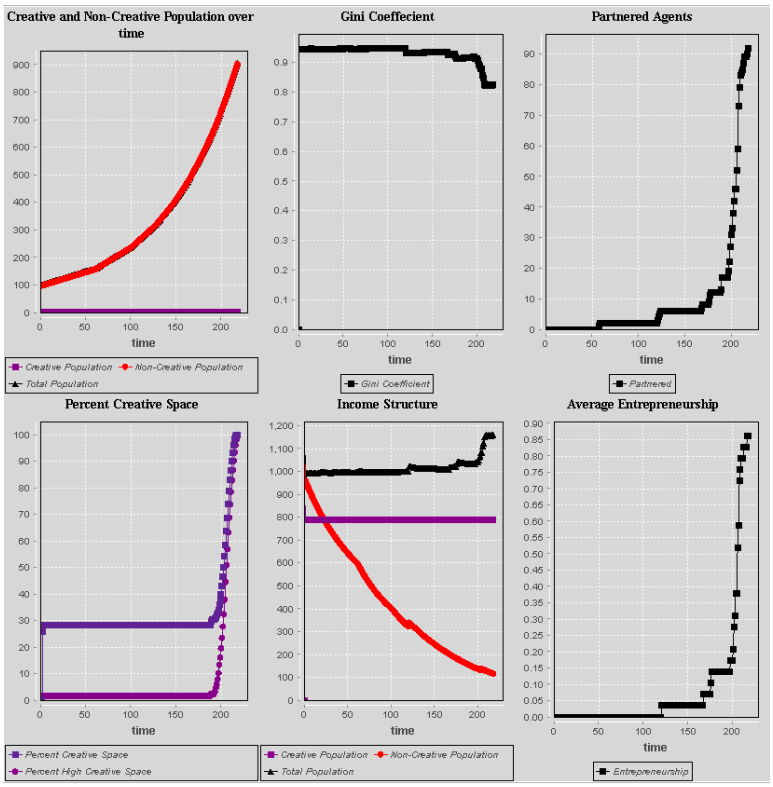


Figure 14: Time series of metrics taken for commercial urban sprawl development configuration after 216 months.

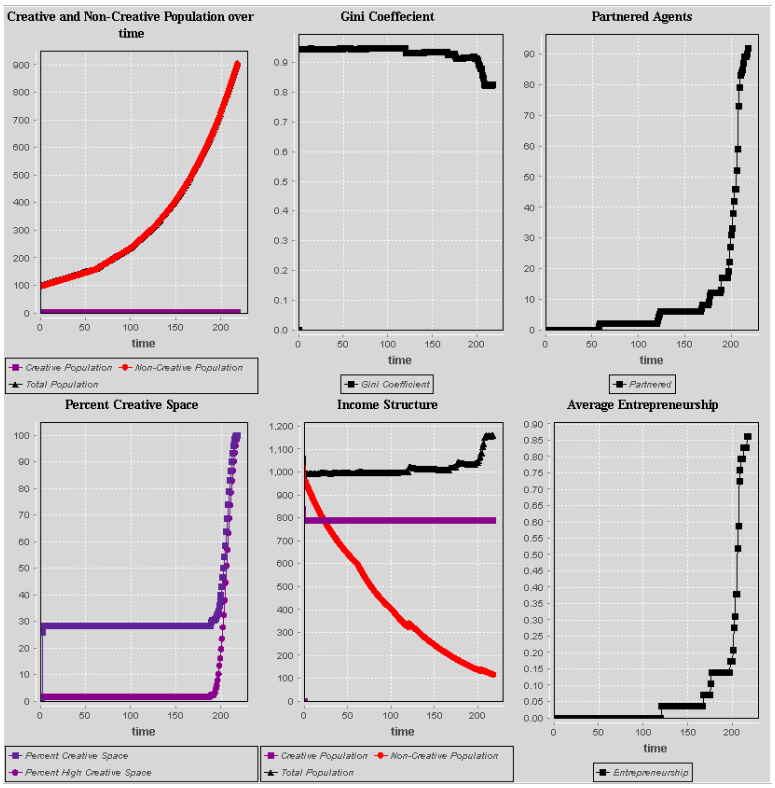


Figure 16: Time series of metrics taken for central urban sprawl configuration after 216 months.

Assessing the Criticality of Germanium as a Byproduct

Nagisa Tadjfar[1], Xinkai Fu[2], Prof. Elsa Olivetti[2]

[1]Student Contributor, Class of 2017, Department of Materials Science and Engineering, Massachusetts Institute of Technology (MIT), Cambridge, MA 02139, USA

[2]Olivetti Research Group, Department of Materials Science and Engineering, Massachusetts Institute of Technology (MIT), Cambridge, MA 02139, USA

Germanium is a byproduct material produced primarily from zinc and coal. Criticality of germanium and its supply risk was assessed using an econometric framework by studying is price elasticities. Annual world production and price data of years 1967-2014 for germanium was used to construct supply and demand models in order to obtain an estimate of the supply elasticity. Several models were tested for and price endogeneity was also tested, but the most appropriate model was selected to be an autoregressive model for both supply and demand. The supply model was constructed with price, zinc production, and 5-year interest rate as shifters along with lag terms for germanium production, germanium price, 5-year interest rate, and zinc production. The adjusted R2 was 0.761 and the long term supply price elasticity was found to be 0.05 with an upper bound of 0.7 and a lower bound of -0.6 indicating that germanium supply is price inelastic. In a similar fashion, a demand model was constructed with two structural breaks accounting for fundamental changes in the market structure in 1991 and 2003, along with lag terms for germanium production, germanium price and antimony price. The adjusted R2 value for the demand model was 0.683 and the price elasticity was 0.05 with an upper bound of 1 and a lower bound of -1 indicating that demand, too, is price inelastic. This creates an added risk for supply shortages, adding to the criticality of germanium. However, the stabilizing behavior of its carriers, coal and zinc, reduce the likelihood of an actual shortage.

INTRODUCTION

Germanium is a high-refractive index, intrinsic semiconductor with unique properties (e.g. IR transparency) that have led to its widespread use in electronic and optical devices. It is also used as a polymerization catalyst for manufacturing polyethylene terephthalate. Its worldwide use in 2015 had the following breakdown: fiber optics, 30%; infrared optics, 20%; polymerization catalysts, 20%; electronics and solar applications, 15%; and other uses, 15% (USGS, 2015). Additionally, germanium is a byproduct material, meaning that rather than being mined for its own sake of germanium production, it is produced as a consequence of major materials. Specifically, byproducts do not influence the profit-maximizing level of production such that price increases of several orders of magnitude are required to break away from being constrained by the carrier production (Lovik, 2016). The two major germanium deposits are Sulphidic Pb–Zn deposits and high-Ge lignite deposits. Therefore, germanium is mostly produced from zinc-smelter residues and high-Ge coal ashes (Frenzel, 2013). Thus, germanium is a byproduct of two carriers, both zinc and coal.

The current standard for assessing the criticality of a given material is to aggregate indicators of supply risk and/or vulnerability, including the concentration of production of a given material in a country or region and the geopolitical risk associated with the region using some combination of world governance indicators. Other metrics frequently used also include substitutability and recyclability. Byproducts are often labeled critical because of an added supply risk compared to minerals produced as main products. Byproducts are therefore frequently identified as minerals that are at a high risk of facing shortages in the near future. Because of shared production costs with the carrier, there is often a large difference between the cost of producing a mineral as a main-product and the cost of producing that same mineral as a byproduct. This can create jumps in the total supply curve during the switch from byproduct to a main product produced on its own (Redlinger, 2016). This indicates that supply may be inelastic with price; given sufficient change in demand, prices may increase drastically without an actual increase in quantity supplied, adding to supply risk and thus criticality of a given mineral. This risk may be further worsened by inelastic demand for the mineral. Furthermore, the supply curve of the byproduct shifts as a result of demand shocks in the carrier market, according to the "by-product effect" (Afflerbach, 2014).

Because of such behavior of byproducts, it is expected that the supply of germanium would be inelastic. Furthermore, because germanium is unique in that it has two carriers rather than one, it is also of interest to explore how coal and zinc production relate, as this may have stabilizing effects on the supply of germanium, lowering supply risk and thus criticality. Despite publications on both geopolitical risks

in criticality assessments as well as geological availability for supply risk (Frenzel, 2013), there is a gap in literature in terms of an economic assessment. The supply inelasticity is worth quantifying when evaluating the criticality of a given mineral and understanding its supply risk. Furthermore, the implications on criticality and price elasticity behavior can help determine policy decisions and inform choices such as recycling rate or investments in new technologies for products that currently use germanium. Thus, the purpose of this research was to quantify supply and demand elasticity for germanium to add an economic component in the ongoing assessment of the criticality of germanium.

METHODS

Partial equilibrium (PE) analysis was used to model interactions in the germanium market under the balance between supply and demand. Supply and demand curves may also shift in ways uncorrelated to demand. In order to account for such shifts, we introduce supply shifters into the model. Similarly, demand shifters were also introduced. In addition to market supply and demand shifters, additional structural breaks were considered to account for stepwise changes in the market. Figure 1 shows the trends in the natural logarithm of germanium production and price over the years 1967-2014. Some non-negligible stepwise shifts in the data can be seen and are rationalized by historical events that occurred. Thus, structural breaks, specifically in the form of demand shifters, were used to account for historical changes in the market structure.

The relationships between supply, demand, and the covariates were modeled using an autoregressive distributed lag (ARDL) model where the potential quantities depend linearly on their previous values and the effects of the regressors are distributed over time. Thus, supply and demand were modeled in the form:

$$Q_t^d = \sum_{q=0}^{Q} \gamma_q^d Q_{t-q}^d + \sum_{p=0}^{P} \alpha_{1,p} P_{t-p} + \sum_{i=1}^{k} \sum_{z=0}^{Z} \alpha_{2,i,z} Z_{i,t-z}^d + \epsilon_t^d$$

$$Q_t^s = \sum_{q=0}^{Q} \gamma_q^s Q_{t-q}^s + \sum_{p=0}^{P} \beta_{1,p} P_{t-p} + \sum_{i=1}^{k} \sum_{z=0}^{Z} \beta_{2,i,z} Z_{i,t-z}^s + \epsilon_t^s$$

Ordinary least squares (OLS) was used to perform backward stepwise regression to select the most statistically significant shifters. Bayesian information criterion (BIC) of the vector autoregressive (VAR) model was used to select the optimal lag order, l. The subset of variables was chosen in order to maximize adjusted R2 of the model. Finally, coefficients were estimated from the best model, from which long run supply elasticity e can be calculated as:

$$e = \frac{\sum_{p=0}^{P} \alpha_{t-p}}{1 - \sum_{q=1}^{Q} \gamma_{t-q}}$$

Data for the variables was collected from multiple databases and reports such as USGS historical statistics and US Board of Governors of the Federal Reserve System, and all analysis was carried out using R.

MODEL

Several supply and demand shifters were proposed based on the standard for a commodity as well as market specifics for germanium. Interest rate was introduced as a supply shifter based on Hotelling's rule for exhaustible resources. Because metal supply is affected by industrial production activities, OECDE IP was also included as a potential supply shifter. Finally, in the context of byproduct metal supply, primary

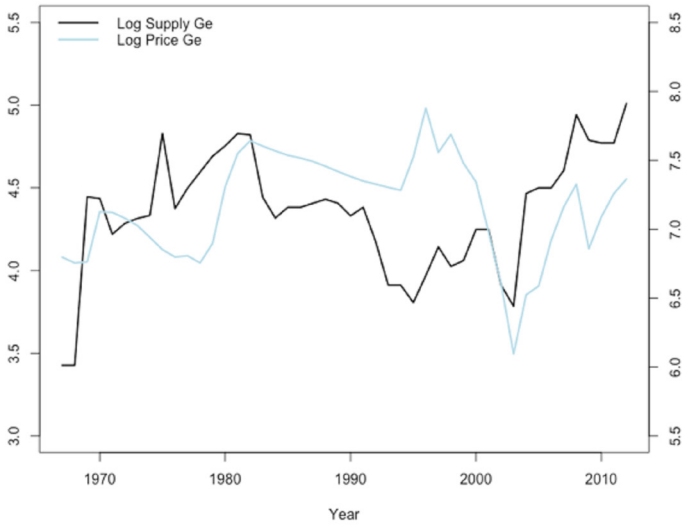


Figure 1: Log of world germanium production and germanium prices from 1967-2014. Vertical shifts can be seen for both at certain years, especially in the market during 1990s.

supply of both zinc and coal were introduced. On the demand side, business cycle and growth indicators were chosen, specifically, S&P 500 and world GDP are both common demand shifters used in such models and were therefore introduced. Prices of major substitutes for germanium were also included. Silicon is a commonly used, less-expensive alternative to germanium in electronic applications and antimony is a substitute of germanium dioxide in the catalysis of the polymerization of polyethylene terephthalate (USGS, 2015). Finally, time was taken to be a common shifter between both supply and demand.

Simultaneous estimation of multiple breakpoints within the time series data was found using an implementation of an algorithm in the package 'strucchange'. The optimal number of breakpoints to include was identified such that the Bayesian information criterion (BIC) estimator was minimized. Two structural breaks were identified in years 1991 and 2003 which align with historical changes in the market that occurred, namely the dot-com bubble in the 1990s as well as the move from sealed bids to negotiated bids in the germanium market in 2003, partitioning the data into three regions as shown in Figure 2. These were added to the demand model in the form of two dummy variables, D_1 and D_2 that take on the value 1 at 1991 and then at 2003 respectively representing upward vertical shifts:

$$D_1 = \begin{cases} 0, & t < 1991 \\ 1, & t \geq 1991 \end{cases}$$

$$D_2 = \begin{cases} 0, & t < 2003 \\ 1, & t \geq 2003 \end{cases}$$

Autocorrelation up to the first lag term was detected in both demand and supply. The most statistically significant shifters along with the appropriate lag terms that maximized adjusted R2 were selected providing the final autoregressive models:

$$\ln(Q_t^d) = \beta_1 \ln(P_t) + \beta_2 \ln(P_{t-1}) + \gamma \ln(Q_{t-1}) + \beta_4 D_{1,t} + \beta_5 D_{2,t} + \beta_4 \ln(P_{Sb,t-1}) + \epsilon_t^d$$

$$\begin{aligned} \ln(Q_t^s) = {} & \alpha_1 \ln(P_t) + \alpha_2 \ln(P_{t-1}) + \gamma_1 \ln(Q_{Zn,t}) + \gamma_2 \ln(Q_{Zn,t-1}) \\ & + \gamma \ln(Q_{t-1}) + \beta_4 \ln(5yIR_{Sb,t}) + \beta_5 \ln(5yIR_{Sb,t-1}) + \epsilon_t^s \end{aligned}$$

It is worth noting that in the above models, price is assumed to be exogenous, meaning that price is assumed to be uncorrelated with the error terms. This is not always true; the coefficient of price may not just

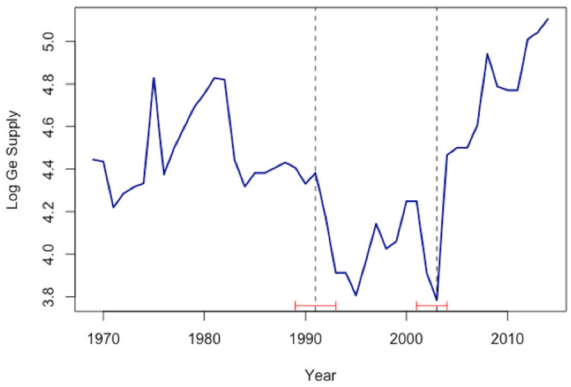


Figure 2: Two structural breaks were identified for the data and added in the years 1991 and 2003 as indicated by the vertical dashed lines.

be capturing the effect of price on demand or supply and an additional indirect change may be included in which case the use of a two-step least squares method is more appropriate. Price endogeneity in germanium was therefore tested for using the demand and supply shifters as instruments, both of which were found to be valid instruments correlating with price using the F-test. However, using the Wu-Hausman test for both supply and demand, price was found to be exogenous.

RESULTS

The coefficients for all the shifters were computed along with their standard errors. The long-term supply and demand elasticities were calculated using the formulas:

$$e_s = \frac{\sum_{p=0}^{P} \alpha_{t-p}}{1 - \sum_{q=1}^{Q} \gamma_{t-q}} \quad \text{and} \quad e_d = \frac{\sum_{p=0}^{P} \beta_{t-p}}{1 - \sum_{q=1}^{Q} \gamma_{t-q}}$$

Because the long-term supply and demand elasticities are functions of several variables extracted from the regression, each with standard errors of their own, propagation of error was used to accurately convey the error in our result. The formula for computing the error in a general function q(x,…,z) of several variables is

$$\delta_q = \sqrt{\left(\frac{\partial q}{\partial x}\delta x\right)^2 + \cdots + \left(\frac{\partial q}{\partial z}\delta z\right)^2}$$

where δx is the random uncertainty corresponding to variable x.

Table 1 below shows the long-term supply and demand elasticities computed along with the upper and lower bounds of the estimates. At 0.05 for both supply and demand, within the confidence interval of 95% they are both found to be price inelastic.

95% confidence	Supply	Demand
Lower Bound	-0.6	-1
Upper Bound	0.7	1
Long-term elasticity	0.05	0.05

Table 1: Long-term supply and demand elasticities along with the upper and lower bounds for germanium were found. Both supply and demand were found to be inelastic.

The interaction between the production of the two carriers, zinc and coal, is of interest to see if the presence of two carriers mitigates or exacerbates supply risk. The Pearson correlation of the differences of historical time series data for zinc and coal production in years 1967-2014 was found to be 0.32. Though a negative correlation would have been ideal to mitigate supply risk, because 0.32 is still relatively small, the existence of two carriers stabilizes the production of germanium, reducing its criticality.

CONCLUSION

Autoregressive supply and demand models for germanium were constructed using USGS data from 1967-2014 using supply and demand shifters as well as two structural breaks for the demand model. Both supply and demand were found to be price inelastic, both having the value 0.05. This increases the supply risk of germanium because inelastic supply suggests that even if prices were driven up by technological breakthroughs, for instance, that shift demand for germanium, the supply will not respond, leaving a shortage. Furthermore, inelastic demand worsens the situation, as demand will not decrease even in the case of extreme price increases. This certainly adds to the criticality of germanium. However, because germanium has two carriers rather than one primary carrier, and the correlations of the differenced time series data for zinc and coal production are not highly correlated, there is a stabilizing effect, reducing supply risk and therefore criticality. Future work includes constructing models for germanium, zinc, and coal to try to predict if an intersection of demand and supply potential will happen and evaluate what situations and assumptions would cause that. Additionally, including recyclability and using the supply and demand elasticities to analyze the displacement of germanium can enhance the model.

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Localizing Laminar Origins of Medial Prefrontal Cortex Neurons With Downstream Projections to the Dorsal Periaqueductal Gray and Nucleus Accumbens in Mice

Isabella Espinel[1] , Caitlin M. Vander Weele[1], Kay M. Tye[1]

[1]Massachusetts Institute of Technology Department of Brain and Cognitive Sciences

Supervisor: Caitlin Vander Weele, Doctoral Candidate, Brain and Cognitive Sciences
Principal Investigator: Kay M. Tye, Ph.D.
Department: Brain and Cognitive Sciences

Ventral tegmental area (VTA) dopamine (DA) neurons and their projections have been of high interest for several decades, since DA is known to mediate many reward related processes. Recently, VTA(DA) projections, particularly projections to the medial prefrontal cortex (mPFC), have become a focus in the field of systems neuroscience. Vander Weele and colleagues have been investigating two downstream mPFC projections (-NAc and –dPAG) in order to understand how these differentially encode aversive vs. rewarding stimuli. Vander Weele and colleagues have observed a difference in the anatomy of these projections in rats as compared to mice. This paper seeks to describe the laminar distribution of identified neuron populations from areas of the medial prefrontal cortex to the nucleus accumbens (NAc) and dorsal periaqueductal gray(dPAG) in mice. Injections of a retrograde path tracer, cholera toxin subunit b, conjugated with AlexaFluor-555, -487, -666 were made into the downstream targets, the NAc and dPAG. NAc projectors (285) are shown to originate in cortical layer 2/3, whereas dPAG projectors (156) originate in cortical layer 5. These data provide new information regarding the anatomical structure of projections which will provide support for current work- investigating the mPFC's role in aversive motivation (Vander Weele et al., 2017 under review). In addition to informing the work of future researchers manipulating these projections, the ultimate goal is to understand how the brain uses these circuits to process motivation, both appetitive and aversive.

1. Introduction

Many neuropsychiatric disorders arise from the dysregulation of brain neurotransmitter systems and subsequently, neural circuit function. For example, dysfunction of the neuromodulator dopamine (DA), involved in motivation and reward-related processes (Robbins et al., 1996) is associated with addiction, depression, Parkinson's Diseases, Huntington's Disease, and schizophrenia. While dopamine systems have been most strongly implicated in mediating reward, more recently DA has begun to be investigated for its potential role in aversive motivation (Salamone 1994, Broussard et al., 2016).

From the 1960s until the mid-2000s, the study of the rodent brain relied on techniques such as lesions, electrical stimulations, pharmacological manipulations, electrophysiology (1980s), microscopy, and basic staining methods (Jessel and Kandel, 1998). However, in recent years, a wide variety of techniques have been developed and refined in order to edit and manipulate organisms' genes. Notably optogenetics was introduced— a method which allows for targeted light activation of cells, and thereby control, of neuronal activity with improved temporal accuracy and a higher degree of selectivity as compared to traditional manipulation tools (e.g., lesion, electrical stimulation, pharmacology). Optogenetics allows experimenters to express light

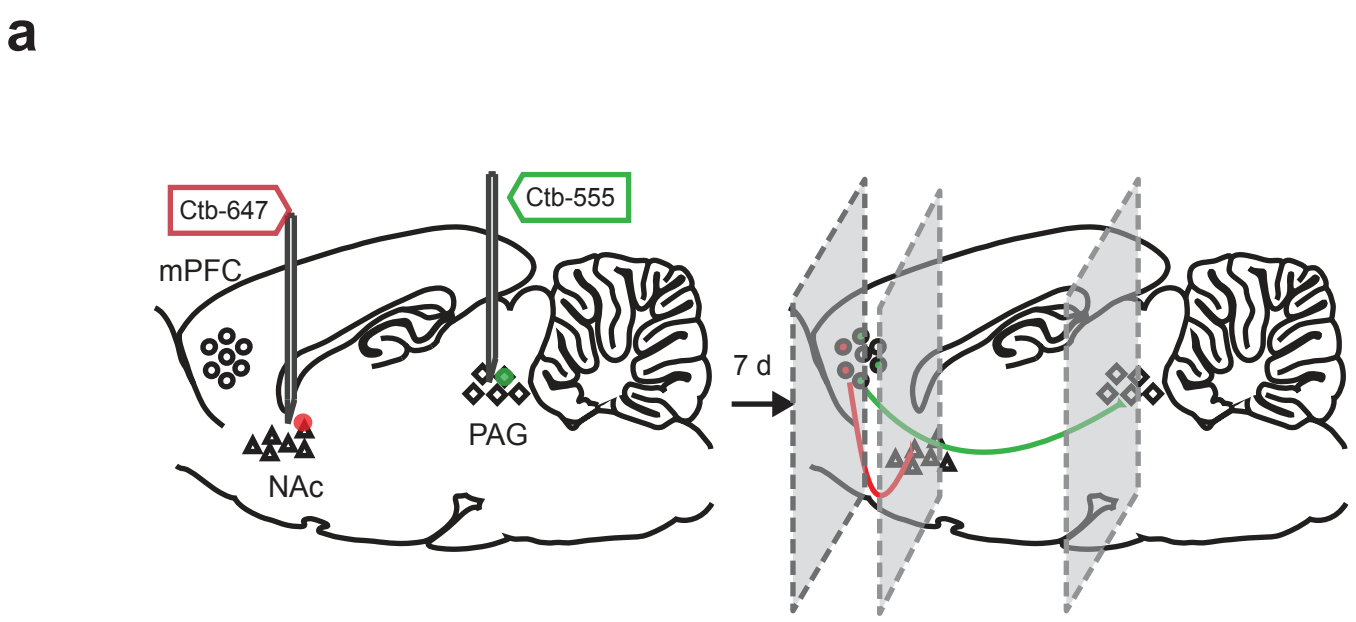

Figure 1. Choleratoxin-subunit b tracing method schematic
(a) Microinjections of choleratoxin-subunit b conjugated to fluorescent protein AlexaFluor -647,-555,-488 (counterbalanced) were injected into either the NAc or the dPAG. These retrogradely labeled cell bodies that projected to either NAc or dPAG resulting in two populations of cells fluorescently labeled in the mPFC. Coronal sections were obtained at the mPFC, NAc, and dPAG for histological verification of injection site.

sensitive opsins, which are membrane-bound channels/pumps, in targeted cell populations which become depolarized/hyperpolarized with light (Boyden et al., 2005, Li et al., 2005). Optogenetics is rapidly becoming the new standard when it comes to manipulating brain circuitry. Moreover, genetic targeting and improved microscopes have combined to give neuroscientists the tools to precisely identify and trace neurons and their projections in ways that were impossible 30 years ago.

The mesolimbic dopamine circuit, comprised of connections between ventral tegmental area (VTA) DA neurons and the nucleus accumbens (NAc) (VTADA-NAc) is characterized for its role in reward and motivation (Ikemoto and Panksepp 1999; Ikemoto 2007; Fiorino et al., 1993). Indeed, DA release in the NAc is thought to underlie reward and positive reinforcement (Ito et al., 2000; Garris et al.,1999). Less studied is the medial prefrontal cortex's role in the modulation of dopaminergic VTA ouput. The mPFC is implicated in cognitive flexibility and decision-making based on stimulus value and expected outcome (Robbins et al.,1989). However, how the mPFC completes these tasks via its communication with downstream structure is still unclear. The mPFC projects to two areas of note, the NAc and the dorsal periaqueductal gray (dPAG). Recent findings show that the NAc projection contrasts the aversive encoding dPAG projection (Vander Weele et al., 2017 in review). More specifically, taken together these pathways provide evidence that VTA DA in the mPFC may be responsible for modulating the mPFC's, and thereby brain's, processing of aversive stimuli.

Though the effects of manipulating these pathways, with –dPAG projections encoding information about aversive stimuli, is still being explored (Vander Weele et al., 2017 in review) the exact anatomy of these projections has not been extensively diagrammed using newer methods. Vander Weele and colleagues noticed that there was a cortical structural difference between mice and rats in these two projections. The laminar structure of the rodent mPFC is slightly different than that of other cortical regions. It lacks an input layer 4, but both deep and superficial cortical layers receive long range inputs and project to other structures (Riga et al., 2014). Vander Weele and colleagues have found that in rats, mPFC-NAc (mPFC- neurons that project to the NAc) and mPFC-dPAG (mPFC- neurons that project to the dPAG) projections originate in layer 5 of the mPFC, which aligns with previous findings (Gorelova and Yang 1996; Gabbott et al., 2005; Ding et al., 2011). In mice, the researchers noted that the mPFC-NAc and mPFC-dPAG projections originated in different layers than in rats. Since there have not been nearly as many projection tracing experiments in mice as in rats, the researchers wanted to further investigate this divergence. This difference could have been due to low/bad expression, viral issues, or simply an inherent structural difference between the mice and rat species.

Therefore, in this paper we seek to characterize the components of these two pathways in mice in greater detail than has been previously attempted. Due to the advancement in viral retrograde/anterograde fluorescent tracers and optogenetic tools, a deeper level of precision in circuitry description is becoming standard (Calloway 2005) and due to

the mPFC-NAc and mPFC-dPAG projections' new proposed roles, there is need for precise characterization of these projections in mice as well as in rats. Moreover, in order to yield efficient results when optically stimulating a projection, optical fibers (300um) must be implanted over the cells of interest. As a result, a priori knowledge of specific cell population locations is integral to any projection stimulation experiment and we seek to provide evidence for the different locations of mPFC-NAc and mPFC-dPAG projectors. The two downstream targets, NAc and dPAG, were identified and retrogradely stained to determine laminar organization of these in the upstream mPFC. It was necessary to determine not only the location of these projections' origins, but also if they collateralized in the mPFC, and if so to what extent. Additionally, results from this project support the work of Vander Weele and colleagues, and provide robust proof that despite the layer origin of these projections, and the reason behind them, the behavioral output of rats and mice is the same when activating this pathway and when observing neuronal activity under both aversive and rewarding conditions.

2. Methods

2.1 animals

Adult wild-type male/female C57BL/6J mice and wild-type Long Evans male rats were used (~22g/~220g; Charles River Laboratories, NC, USA), and they were group housed on a normal 12h:12h light/dark cycle (lights on at 09:00 AM). All experiments involving the use of animals were in accordance with NIH guidelines and approved by the MIT Institutional Animal Care and Use Committee.

2.2 general virus surgery

For all subjects, surgeries were performed under aseptic conditions and body temperature was maintained with a heating pad. Rodents were anesthetized with isoflurane mixed with oxygen (5% for induction, 2.5-2% for maintenance, 1L/min oxygen flow rate) and placed in a digital small animal stereotax, equipment used in head-fixed surgeries (David Kopf Instruments, Tujunga, CA, USA). Following initial induction, hair was removed from the dorsal surface of the head with hair clippers, ophthalmic ointment was applied to the eyes, the incision area was scrubbed with alcohol pads and betadine (x3 each), and 2% lidocaine was injected just under the skin surface above the skull for topical anesthesia. All measurements were made relative to bregma for virus surgeries. Viral injections were performed using a beveled microinjection needle (26-gauge rat, 33-gauge mice) with a 10 µL microsyringe (Nanofil; WPI, Sarasota FL, USA) delivering virus at a rate of 0.05 µL/min using a microsyringe pump (UMP3; WPI, Sarasota, FL, USA) and controller (Micro4; WPI, Sarasota, FL, USA). For injections at multiple locations on the dorsal-ventral axis, the most ventral location was completed first and the injection needle was immediately relocated to the more dorsal location and initiated. After injection completion, 15 mins were allowed to pass before the needle was slowly withdrawn. After viral infusions were completed, craniotomies were filled with bone wax and the incision closed with nylon sutures. Subjects were maintained under a heat lamp and provided 0.05 mg/kg (rat), 0.10 mg/kg (mouse) buprenophine (s.c., diluted in warm Ringers solution) until fully recovered from anesthesia.

2.3 retrograde Cholera toxin-b tracing

Rodents were prepared for stereotaxic surgery as described above. Briefly, 350 nl of Cholera Toxin subunit B (CTB) conjugated to Alexa Fluor-488, 555, or 647 (Molecular Probes, Eugene, OR, USA) was injected into the dorsal periaqueductal gray (dPAG; AP: -4.2, ML: -0.5; DV: -2.4 mm) and NAc shell (AP: +1.0, ML: +0.75, DV: -4.5 mm) (color counterbalanced between animals).

After 7 days, mice were transcardially perfused and histologically prepared (under Perfusion and Storage). Z-stack stitches, collations across Z axis, encompassing both prelimbic (PL) and infralimbic (IL) regions of the mPFC were acquired using a scanning confocal microscope (Olympus FV1000) with Fluoview software (Olympus, Center Valley, PA, USA) under a 40x/1.30 NA oil immersion objective. Quantification of fluorescence intensity across layers was accomplished by analyzing 200w x 400h µm sections encompassing ventral PL / dorsal IL across mPFC layers based on DAPI density/morphology in FIJI ImageJ. Sections were normalized to the section with peak fluorescence within subjects. For cell quantification, the number of CTB positive (441) and double-positive (17) neurons were counted in both the IL and PL subregions of the mPFC using FluoView software (Olympus, Center Valley, PA).

3. Histology

Perfusion and storage. Subjects were deeply anesthetized with sodium pentobarbital (200 mg/kg; i.p.) and transcardially perfused with 15 mL (mouse) / 60 mL (rat) of Ringers solution followed by 15 mL/ 60 mL (rat) of cold 4% paraformaldehyde (PFA) dissolved in 1x PBS. Animals were decapitated and the brain was extracted from the cranial cavity and placed in 4% PFA solution and stored at 4 °C for at least 48 hrs. 36 hours before tissue sectioning, brains were transferred to 30% sucrose solution dissolved in 1x PBS at room temperature. Upon sinking, brains were sectioned at 40 µm (mouse) / 60 µm (rat) on a freezing sliding microtome (HM420; Thermo Fischer Scientific). Sections were stored in 1x PBS at 4 °C until immunohistochemical processing.

Slice preparation. Sections were incubated in 1x PBS - 0.3% Triton containing 3% normal donkey serum (Jackson ImmunoResearch, West Grove, USA) and DAPI (1:50,000) for 1 hr. Sections were washed 4 times (10 min each) in 1x PBS and mounted onto glass slides. Slices were allowed to dry and were coverslipped using polyvinyl alcohol (PVA) mounting medium with DABCO (Sigma, MO, USA).

Confocal microscopy. Fluorescent images were captured using a confocal laser scanning microscope (Olympus FV1000), with FluoView software (Olympus, Center Valley, PA), under a dry 10x / 0.40 NA objective, a 60x/1.42 NA oil immersion objective, or a 40x /1.30 NA oil immersion objective. The location of injection site was determined by taking serial z-stack images through the 10x objective across a depth of 20-40 µm, with an optical slice thickness of 5-8 µm. High magnification images fluorescence quantifications were obtained through the 40x or 60x objective using serial z-stack images with an optical slice thickness of 3-4 µm (5 slices) using matched parameters and imaging locations. Fluorescence (in arbitrary units) was obtained from analysis in FIJI ImageJ. For quantification of fluorescence across layers in the mPFC, measurements were normalized to the z-stack containing the maximum value.

4. Results

Cholrea toxin subunit-b (CTB) conjugated with fluorescent proteins was used to retrogradely label mPFC-NAc and mPFC-dPAG projectors in both the mouse and rat. A depiction of the technique used to achieve this is featured in **Figure 1**. Results from Vander Weele and colleagues found that in rats, dPAG projectors originate primarily in layer V and NAc projectors in mostly layer 5, with some in layer 2/3 **(Figure 2 a-e)**. These findings aligned with previous retrograde studies. Vander Weele and

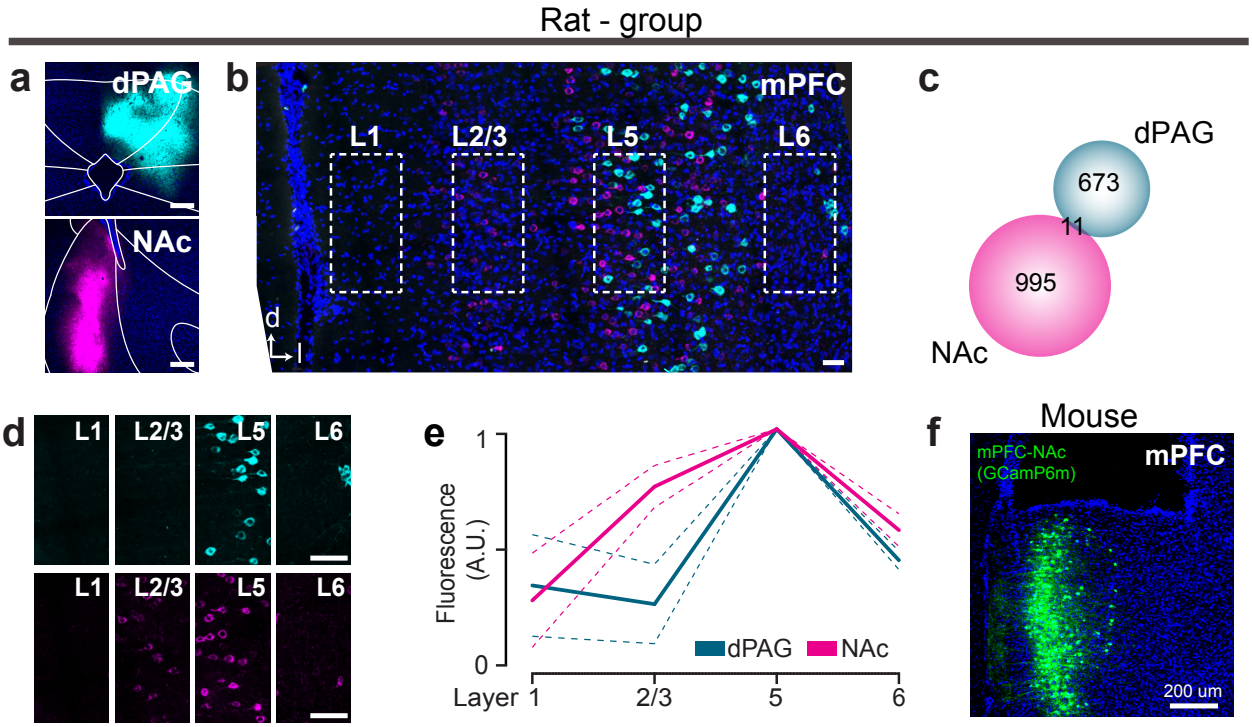

Figure 2. Rat mPFC-NAc and mPFC-dPAG projectors form unique, non-overlapping populations originating in layer 5. **(a)** Histological verification of correct injection site in both the dPAG and NAc in the rat. **(b)** Confocal image of the rat mPFC at 40x with dPAG projectors labeled in cyan and NAc projectors labeled in magenta. Few cells (mean = 1.57 per slice) were CTB co-labeled suggesting that the two projectors (mPFC-NAc mean = 96.14 per slice, mPFC-dPAG mean = 142.14 per slice) do not collateralize and project to each other. **(c)** Quantification of cell bodies labeled as NAc vs. PAG projectors only 11 out of 1,679 CTB+ cell bodies were dual-labeled for CTB. **(d)** Layer specific breakdown of both projector populations in the mPFC. Fluorescence quantification of these revealed that the distribution of cell bodies varied across cortical layers in the rat mPFC. **(e)** dPAG- projectors originate predominately from layer 5 while NAc projectors mostly originate in layer 5, but also layer 2/3. **(f)** Representative histological image of a mouse subject used in Vander Weele et al. single cell epifluorescent in vivo calcium imaging experiments. GCaMP6m was used as a proxy for cell activity in the mPFC. Cells labeled are NAc-projectors, qualitatively we see majority of projectors are in layer 2/3. Error bars indicate SEM. Scale bars± 100 um.

colleagues conducted in vivo epifluorescent calcium imaging experiments in mice in order to image real-time dopamine release in both NAc and dPAG projectors in the mPFC. The mice were allowed to self-administer sucrose or received a shock through the chamber floor. Epifluorescence, as a proxy for cell response, was recorded and analyzed. In this experiment, dPAG projectors demonstrated increased fluorescence in response to aversive stimuli while NAc projectors were more sensitive to rewarding stimuli, aligned with Vander Weele's predictions. In other words, these populations differentially respond to aversive and rewarding stimuli. Upon histological verification of GCaMP6m expression, researchers discovered a discrepancy in the layer localization of mPFC neurons in these experiments compared to retrograde tracing studies done in the rat (**Figure 1 f**). In the mice NAc projectors seem to originate in layer 2/3 of the mPFC, while dPAG projectors, in rats, originate in layer 5. To verify these results the same CTB retrograde tracing methodology was repeated on mice (n = 2). Images from a representative mouse are shown in (**Figure 3 a-e**). NAc projectors originate mostly in layer 2/3 of the mPFC while dPAG projectors are in layer 5, corroborating observed differences in in vivo calcium imaging. Similar distribution and co-labelization rates are observed in mice as in rats (**Figure 3 f**), few co-labeled cells indicate these two subpopulations do not project to each other.

5. Discussion

This study presents novel data about the architecture of the mouse mPFC-NAc and mPFC-dPAG projections. The results present a structural difference between the mouse and rat mPFC-NAc projectors. As part of the larger work for Vander Weele and colleagues this study sought to answer questions that arose from Vander Weele's efforts to determine dopamine's role on distinct prefrontal circuits. Particularly, the researchers were interested in determining if this structural difference was present across animals. Results showed that the difference was common across animals. Results also provide valuable information about these cell's locations in the mouse mPFC.

First, researchers conducted CTB tracing in a rat to corroborate previous work in literature (Gabbott et al., 2005; Ding et al., 2001;

Vertes, 2004). Following the execution of a novel technique in mice, in vivo calcium imaging, standard verification procedures revealed a previously unidentified difference in mPFC-NAc projectors in rat and mice. The results of this histological verification provided the impetus for researchers on Vander Weele's team to further examine the results.

After first note of the difference, Vander Weele and colleagues needed to determine if the observed difference was common to all mice or if it was the result of injection site sensitivity, or other experimental abnormalities. The results of these further investigations revealed an interesting anatomical difference between the two species. In this study we find that the two species have different layers of origin with rat -NAc projectors originating in layer V and mice in layer II/III. These architectural differences could be cause for concern, as we do not fully understand what they could be indicative of, perhaps a behavioral difference. Jonckers and colleagues (2011) found that there are some functional connective differences, though few, between the two species when rsfMRI imaging these animals in analogous regions, suggesting these connective differences could lead to behavioral differences. Therefore, it was important to determine if a similar situation could be present in this experiment.

The study that led to the uncovering of this interesting discrepancy, in vivo calcium imaging, also confirms that these two distinct subpopulations are, in fact, responsible for the same behavioral outputs in both species. During Vander Weele's in vivo calcium imaging, mice were either delivered a foot shock, or allowed to self-administer a sucrose solution. These two stimuli are considered aversive and rewarding, respectively. What was found in this study is that the activation of the two populations corresponded with the same behavioral output found in rats when these projections were optogenetically stimulated. That is, when stimulated in rats, the dPAG projection elicited aversive behaviors like freezing, burying, and escape-related behaviors in rats as compared to the NAc projectors. We believe, then, that though this difference exists in the two species, the populations contribute to similar behavioral outputs in line with previous work (Brandão et al., 2008; Peters et al., 2008).

A deeper understanding of why this difference exists was not the goal of this paper, and was not examined, but could be a point of interest in the future. Despite small sample size (n = 2), it is known that architecture (Paxinos et al., 2004) doesn't vary largely from animal to animal, but cohort size should be expanded to improve statistical significance. Importantly, this study uncovered a difference between two commonly used research species for a popular pathway of study. This study will allow future researchers to accurately account for this difference when imaging, stimulating and analyzing data related to these projections.

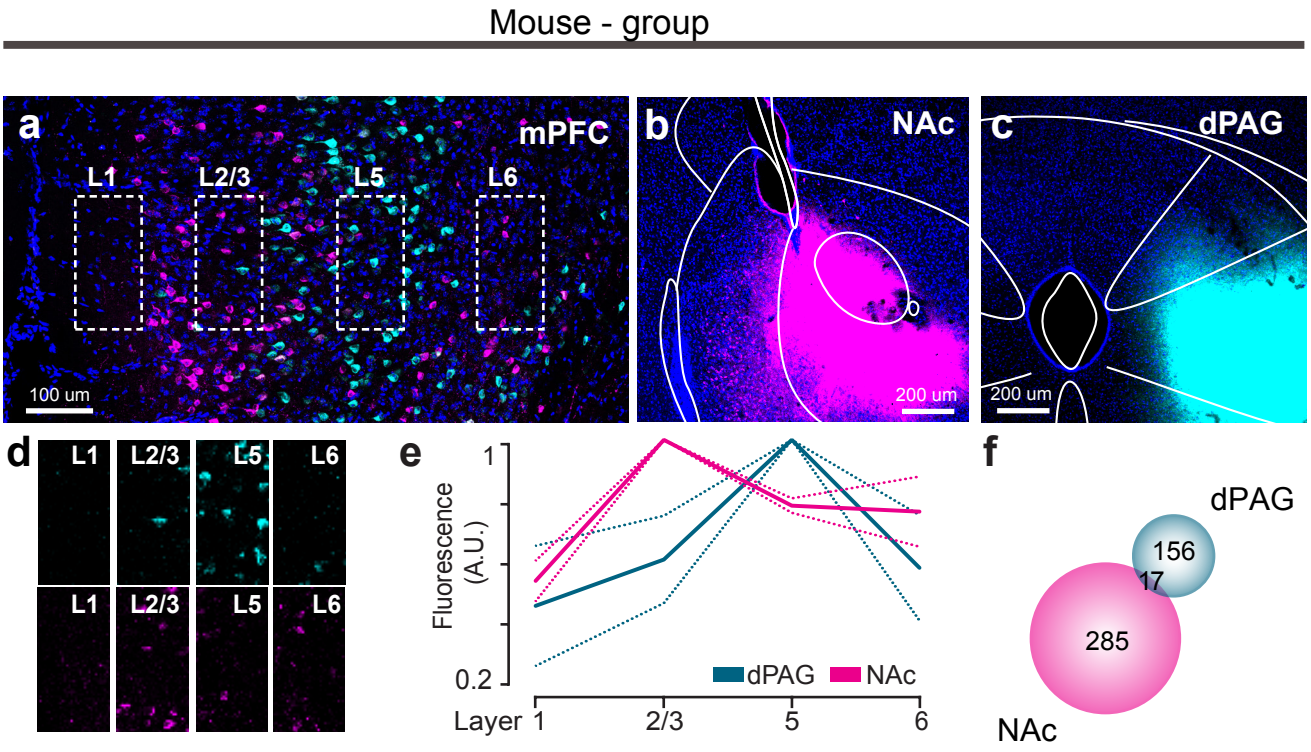

Figure 3. Mouse mPFC-NAc and mPFC-dPAG projectors form unique, non-overlapping populations originating in layer 2/3 for NAc projectors and layer 5 for dPAG.

(a) Representative image of the mouse mPFC with CTB+ NAc & dPAG-projectors (mPFC-NAc mean = 142.5 per slice, mPFC-PAG mean = 78 per slice) labeled in magenta and cyan, respectively. Layers outlined and few cells (mean=8.5) appear to be co-labeled reassuring that in mice, as well as rats, these cells do not collateralize and project to each other. **(b)** Histological verification of CTB microinjection site in NAc 10x confocal microscopy image. **(c)** Histological verification of dPAG CTB microinjection. 10x confocal image. **(d)** NAc-projectors originate mostly in layer 2/3 and dPAG-projectors mostly originate in layer 5 (n=2). **(e)** dPAG- projectors originate predominately from layer 5 while NAc projectors mostly originate in layer 2/3. **(f)** Quantification of cell bodies labeled as NAc vs. PAG projectors only 17 out of 441 CTB+ cell bodies were dual-labeled for CTB. Error bars indicate SEM.

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